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Contents on Inside Cover

American Heart Journal

CONTENTS FOR DECEMBER, 1954

Original Communications

Page

Cardiac and Pulmonary Artery Pressure Pulses in Experimental Mitral Stenosis. Richard P. Lasser, M.D., and Leo Loewe, M.D., New York, N. Y. 801

Intracardiac Left-to-Right Shunt With Pulmonic Stenosis. Abraham M. Rudolph, M.D., Alexander S. Nadas, M.D., and Walter T. Goodale, M.D., Boston, Mass. 808

The Effect of Blood Pressure Reduction With Arfonad on Renal Hemodynamics and the Excretion of Water and Electrolytes. John H. Moyer, M.D., W. R. Livesay, M.D., and Richard A. Seibert, Ph.D., Houston, Texas 817

Clinical Calibration in Phonocardiography. Aldo A. Luisada, M.D., and Giorgio Gamna, M.D., Chicago, Ill. 826

Sonvelographic Recording of Murmurs During Acute Myocarditis. Robert F. Rushmer, M.D., Robert A. Tidwell, M.D., and Richard M. Ellis, B.S., Seattle, Wash. 835

Studies With the Displacement, Velocity, and Acceleration Ballistocardiograph in Aortic Insufficiency. J. E. Smith, M.D., Robert Rosenbaum, M.A., and Ralph Ostrich, A.M., Washington, D. C. 847

Factors Affecting the Low-Frequency, Critically-Damped Ballistocardiogram, With Special Reference to Age, Body Size, and Body Composition. Henry Longstreet Taylor, Ph.D., William F. Maloney, M.D., and Ancel Keys, Ph.D., Minneapolis, Minn. 864

Quantitative Estimation of Ventricular Strain in the Limb Leads. Desiderio Gross, M.D., Santiago, Chile 881

A Mathematical Method To Determine the Magnitude of Electrical Axis. Carlos Ayala y de Landero, Guadalajara, Mexico 894

Thoracic Ballistocardiography. John N. Edson, M.D., Gerald H. Flamm, M.D., Robert Dickes, M.D., Michael Tobin, M.E.E., and Laurence Loeb, M.D., Brooklyn, N. Y. 897

Provocative Aspects of Lipotropic Therapy in Angina Pectoris. Norman E. Goulder, M.D., R. W. Kissane, M.D., and Robert W. Bohl, M.D., Columbus, Ohio 906

Flarimeter Tests on Athletes. P. V. Wells, D.Sc., Princeton, N. J. 914

The Portal Venous Pressure in Organic Heart Disease. Esmé M. Wren, M.D., Liverpool, England 929

The Control of Certain Cardiac Arrhythmias With Isopropylnorepinephrine. E. E. Schumacher, Jr., M.D., and C. L. Schmock, M.D., Detroit, Mich. 933

Index

Index 941

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American Heart Journal

VOL. 48 DECEMBER, 1954 NO. 6

Original Communications

CARDIAC AND PULMONARY ARTERY PRESSURE PULSES IN EXPERIMENTAL MITRAL STENOSIS

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NEW YORK, N. Y.

THE relationship between pulmonary artery pressures and the level of pressure within the left atrium has been a subject of considerable recent interest. Studies of this relationship in human beings by means of cardiac catheterization, particularly the recording of pulmonary artery "wedge pressures," are, in pathologic states, complicated by the existence of variable resistance within the pulmonary vascular bed and variable myocardial function. This investigation has therefore been undertaken in animals to determine the response of the pulmonary artery pressure to acute elevation of left atrial mean pressure in the absence of such additional variables. The elevation of left atrial pressure is accomplished by the surgical production of a simulated mitral stenosis. The technique employed, developed independently at this laboratory, has also been described by Ellison and associates[1] and Ankeney.[2] It is possible to achieve a finely graded and considerable elevation of the pressure within the left atrium. This is attainable without diminution of the systemic or left ventricular systolic pressure. The electrocardiogram which is recorded simultaneously remains unaltered or develops only minor abnormalities at severe degrees of stenosis. Thus, the conditions for an adequate experimental mitral stenosis, which were stipulated by Katz and Seigal in 1931, have been maintained. These are (1) that there should be no constriction of the coronary circulation which might impair ventricular contractility; (2) that concomitant aortic stenosis should not be inadvertently produced; and (3) that the cavity of the left ventricle should not be distorted.

The hearts of all of the preparations were examined at the conclusion of

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each experiment, and the absence of either coronary artery constriction or aortic stenosis was verified. This constituted both a physiologic and anatomic check. The double verification is considered necessary because the presence or absence of coronary insufficiency during the experimental situation is difficult to determine from post-mortem examination alone but is readily evidenced in the electrocardiogram.

Our experience with this technique has been that marked coronary insufficiency and impaired myocardial function occasionally may develop with moderate or marked degrees of mitral stenosis in the presence of a maintained systemic pressure and in the absence of obvious mechanical interference with the coronary circulation. This fact, not hitherto observed, may account for some of the contradictory findings which previous investigators have reported in experimental mitral stenosis.[3-9]

METHOD

Adult dogs were anesthetized with intravenous Nembutal. Intermittent positive pressure oxygen insufflation was administered intratrachially by means of a Pneumatic Balance Respirator.* The chest was opened on the left side. Cardiac catheters (#8F) were inserted into the pulmonary artery in retrograde fashion through a secondary branch in the left upper lobe, into the left atrium through a pulmonary vein of the same left upper lobe, and into the left ventricle or aorta through the left subclavian artery. Pressure recordings in the pulmonary artery and left atrium were made with Sanborn electromanometers. The ventricular or aortic pressure was registered with a Statham strain gauge. Tracings were made by a Sanborn direct-writing four-channel polyvisocardiograph.

Technique of Suture.—The pericardium was opened longitudinally, medial to the phrenic nerve. The heart was gently rotated to the animal's right to expose the posterior surface. The location of the interatrial septum on the posterior surface was determined by palpation and further confirmed by the identification of the inferior vena cava. The interatrial septum was palpated on the anterior surface of the atria by placing the forefinger underneath the arch of the pulmonary artery. The anterior and posterior walls of the atria were then pressed together between the thumb and forefinger. A suture was passed through the interatrial septum from back to front and placed so as to lie just above the atrioventricular groove. Since this suture was subject to considerable tension when mitral stenosis was created, the following precaution was employed to prevent tearing of the normally friable atrial wall and to control often troublesome bleeding. The suture was looped about a short length of cotton roll which was thus interposed between the knot and the atrial wall. The free ends of the posterior strands were led around to the anterior surface and tacked in place just above the A-V groove. The strands from the posterior and anterior surfaces were both threaded through a short length of polyethylene tubing. Any traction on these strands produced a purse-string effect at the base of the left atrium just above the A-V groove. Any degree of narrowing of the atrial outflow orifice could be produced and maintained simply by placing

*Mine Safety Appliance Co., Pittsburgh, Pa.

a hemostat across the suture strands. Considerable tension could be applied without tearing the sutures from the atrial wall because of the presence of the interposed cotton roll. Proper placement of the key suture at or near the intratrial septum could be effected with a minimum of practice. When the suture was properly placed, there was no gross interference with coronary circulation, no distortion of the aortic outflow tract, no obstruction to the coronary sinus, pulmonary veins, or vena cava. All of the effects noted therefore can be considered to be the result of the sudden interposition of a resistance to flow just above the annulus of the mitral valve.

RESULTS

The relationship between left atrial mean pressure and pulmonary artery systolic and diastolic pressure for each individual animal experiment is shown graphically in Fig. 1. The form of all of these curves is roughly similar, indicating that acute elevation of the mean pressure within the left atrium always results in a rise in both the systolic and diastolic pressure within the pulmonary artery. A more explicit analysis of this relationship is shown in Fig. 2. This graph has been plotted so as to show the relationship of the pressure-increment-ratio $\frac{\Delta P_{PA}}{\Delta P_{LA}}$ (ordinate) to left atrial mean pressure. Ordinate values have been calculated separately for each pressure range during successive increases in left atrial mean pressure from 5 to 10 mm. Hg, 10 to 20 mm. Hg, 20 to 30 mm. Hg, 30 to 40 mm. Hg, 40 to 50 mm. Hg, and 50 to 60 mm. Hg. The term ΔP_{PA} refers to the average pressure increment observed in the pulmonary artery of all experiments. The term ΔP_{LA} refers to the average pressure increment observed in the left atrium in all experiments. Thus a value of "1" indicates a rise in pulmonary pressure equal to that of left atrial mean pressure, without reference to the absolute levels of pressure.

From this plot it can be seen that when left atrial mean pressure is elevated from a level of 5 mm. Hg to 10 mm. Hg, pulmonary artery systolic pressure rises an average of 0.6 mm. Hg for each 1 mm. Hg rise in the left atrium. The range of variation is from 0.3 mm. Hg to 0.9 mm. Hg. Diastolic pressure rises 0.68 mm. Hg for each millimeter rise of left atrial pressure, with a range of variation of 0.4 to 1.0 mm. Hg. The average pulmonary artery pulse pressure therefore falls slightly.

Elevation of left atrial pressure from 10 to 20 mm. Hg results in a rise of pulmonary artery systolic pressure by an average of 0.65 mm. Hg for each millimeter of left atrial pressure. The range of variation is from 0.40 to 0.90 mm. Hg. Pulmonary artery diastolic pressure rises 0.77 mm. Hg for each millimeter of left atrial pressure. The range of variation is from 0.55 to 0.9 mm. Hg. The effect of elevation of left atrial pressure at this pressure level again results in a decline in the average pulse pressure. When left atrial pressure is elevated from 20 to 30 mm. Hg, the average increment in pulmonary artery systolic pressure becomes greater than the diastolic pressure increment and pulse pressure rises. Further elevations of left atrial pressure from 30 to 40 mm. Hg and

from 40 to 50 mm. Hg result in a progressive increase in the magnitude of the increment ratio of pulmonary artery systolic pressure. At these levels, the rise in the left atrial pressure is reflected in an entirely equal rise in pulmonary artery systolic pressure. The average increment in diastolic pressure is not as great as that of the systolic pressure, and pulse pressure progressively increases. Finally, at the very high levels of left atrial pressure of 50 mm. Hg,

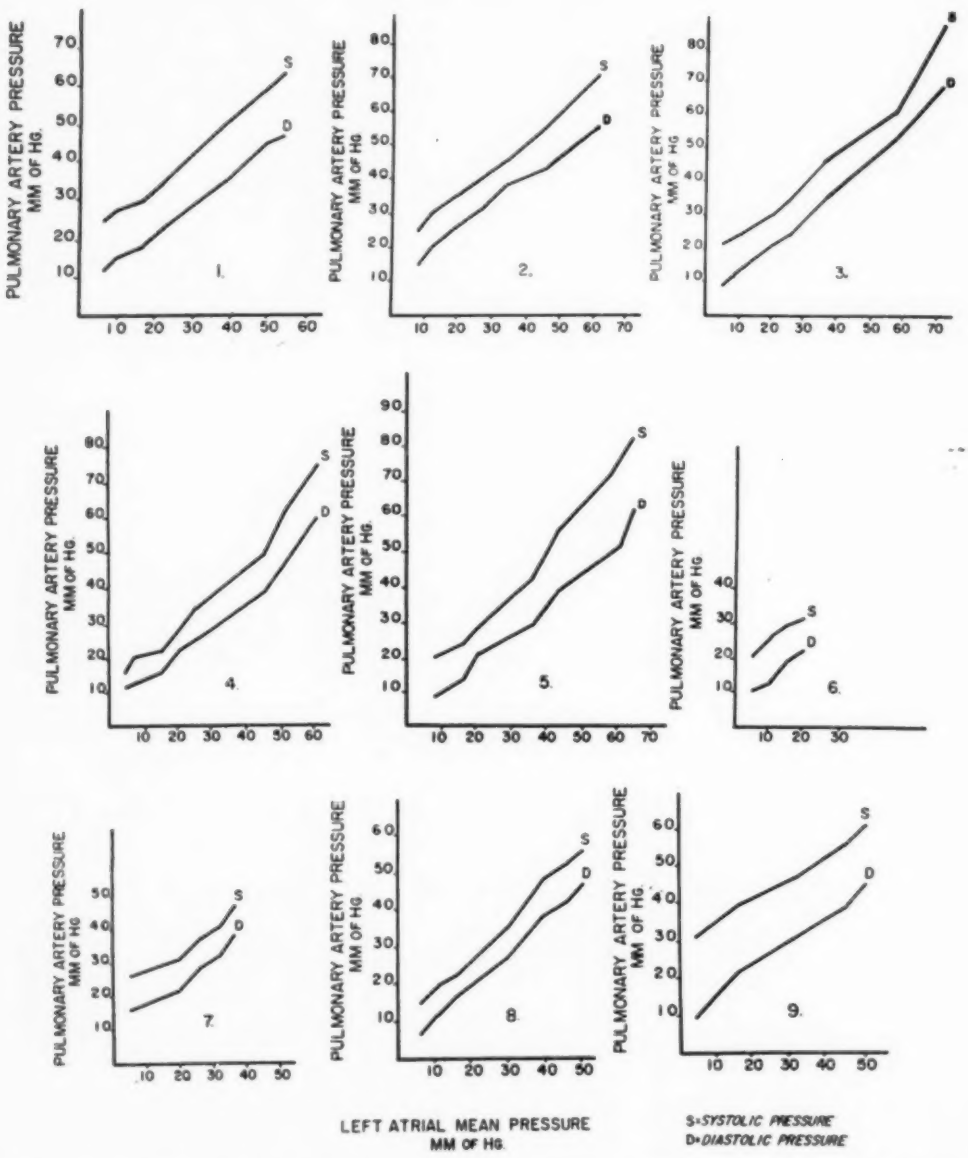

Fig. 1.—Demonstrates the relationship which exists between pulmonary artery systolic and diastolic pressure and left atrial mean pressure during increasingly severe constriction of the mitral valve orifice in each of the nine experiments.

the further elevation to 60 mm. Hg results in an increment of pulmonary artery systolic pressure of 1.14 mm. Hg for each millimeter rise in left atrial pressure. The average increment in diastolic pressure also rises but not as much as that of the systolic increment, and the pulse pressure therefore widens further.

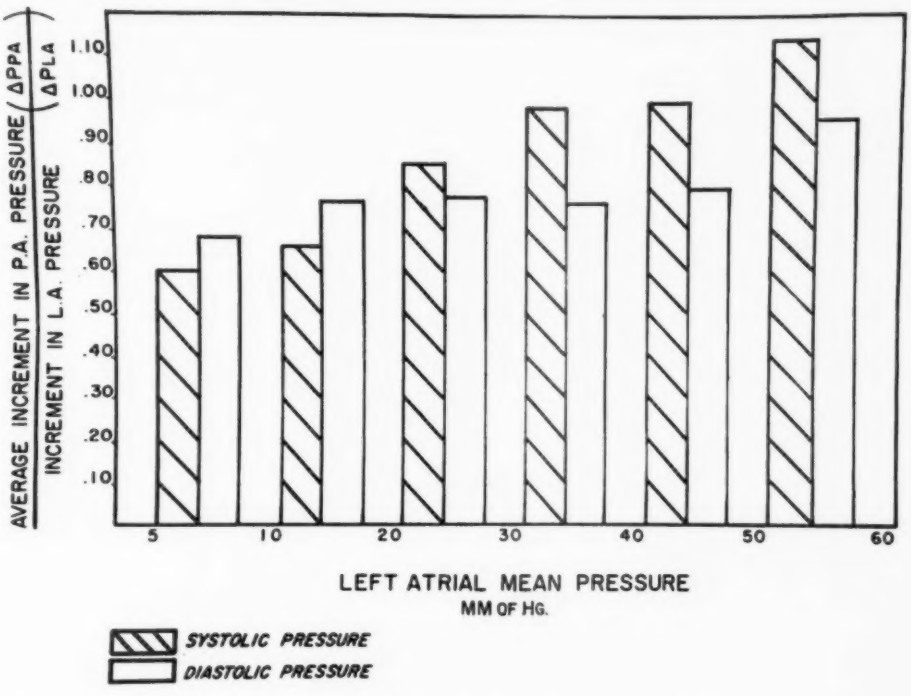

Fig. 2.—Summary of the average results of the individual experiments. The graph is in terms of the average rise in pressure within the pulmonary artery for each millimeter rise in pressure within the left atrium at the various levels of atrial pressure shown.

When the absolute values of the pulmonary artery systolic and diastolic pressures are compared with mean left atrial pressures, it is observed that the pulmonary artery diastolic pressure is occasionally exceeded by left atrial mean pressure. This occurs when pressures are in the range of 40 to 60 mm. Hg. The extent of the difference is from 4 to 8 mm. Hg. Such an observation raises the possibility of retrograde flow in the vascular system. To explore this aspect of the situation, measurements of instantaneous pressures, stimultaneously obtained, were made three times during a single cardiac cycle, namely, at the end of diastole, the peak of the pulmonary artery pressure, and the peak of the "v" wave in the left atrium. These values are shown in Table I. It can be seen that pulmonary artery pressure exceeds left atrial pressure by a wide margin during most of systole and generally by a small margin during most of diastole except at the time of the height of the "v" wave. Thus a pressure gradient driving flow in an orthograde direction exists during most of the cardiac cycle with possibly some momentary retrograde flow in early diastole. The presence

of a markedly elevated "v" wave in the left atrial pressure pulse was found rather characteristically to occur at high pressure levels.

TABLE I. INSTANTANEOUS PRESSURES IN THE LEFT ATRIUM AND PULMONARY ARTERY

	END DIASTOLIC PRESSURE (MM. HG)	PULMONARY ARTERY SYSTOLIC PRESSURE (MM. HG)	PEAK OF LEFT ATRIAL "V" WAVE (MM. HG)	LEFT ATRIAL MEAN PRESSURE (MM. HG)
1. LA*	47.7	51.1	58.8	52.2
PA†	48.8	64.4	57.7	
2. LA	55.0	57.5	72.5	60
PA	55.5	72.2	67.7	
3. LA	63.7	65	86.5	72.5
PA	66.2	87.5	83.7	
LA	50.0	52.2	68.8	58.8
PA	53.3	70.0	70.0	
5.				
LA	56.6	57.7	77.7	66.6
PA	60.0	81.6	80.0	
9. LA	40.0	42.5	60.0	48.7
PA	43.5	60.0	51.2	

*LA = Left Atrial Pressure
†PA = Pulmonary Artery Pressure

Right ventricular systolic pressure, in the absence of pulmonary stenosis, is equal to pulmonary artery systolic pressure. Therefore, it may be stated that experimental mitral stenosis uniformly produces systolic hypertension within the right ventricle. Actual measurement of pressure within the right ventricle has been performed in several instances, and the systolic pressure has been observed to increase with increases in left atrial pressure in a manner similar to the response of the pulmonary artery systolic pressure which has been described previously. Thus, experimental mitral stenosis results in right ventricular hypertension similar to that seen in mitral stenosis in human beings.

This very consistent development of pulmonary hypertension has not been observed by all previous investigators. It is believed that the absence of pulmonary hypertension during experimental mitral stenosis is explained as the result of the development of severe coronary insufficiency during the procedure. Such coronary insufficiency has been found frequently with this particular method of producing acute mitral stenosis even though the purse-string suture around the base of the left atrium does not obviously constrict any of the coronary vessels. Moreover, electrocardiographic evidence of coronary insufficiency has been found to develop with conspicuous degrees of mitral stenosis in the presence of a well-maintained left ventricular systolic pressure. It is possible that these electrocardiographic changes are the result of obstruction to the coronary sinus outflow. Whatever might be the cause of the coronary insufficiency, the effect observed is that of a failure to maintain elevated pulmonary

artery and left atrial pressures. This is believed to be the result of "failure" of the right ventricle, since this fall in left atrial pressure has been found to be accompanied by a concomitant rise in the right atrial pressure.

Studies in five animals on the behavior of right atrial pressure during acute mitral stenosis have revealed that the pressure in this chamber is not altered or at most rises by 1 or 2 mm. Hg at a time when the left atrial pressure is maintained at very high levels (40 to 60 mm. Hg). As previously mentioned, however, should electrocardiographic evidence of myocardial hypoxia develop (QRS, ST segment, and T-wave changes) then right atrial pressure rises markedly, left atrial pressure falls sharply, and systemic pressure declines.

SUMMARY

The response of pulmonary artery systolic and diastolic pressure to acute elevation of left atrial mean pressure has been explored in animals with an open chest. The elevation of pressure within the left atrium has been effected by the production of simulated mitral stenosis. Observations were made only in the presence of a well-maintained systemic pressure level and in the absence of observable myocardial ischemia. Under these conditions, pulmonary hypertension was uniformly observed throughout all levels of elevation of left atrial pressure. The individual responses of the pulmonary artery systolic and diastolic pressures have been detailed.

The observation has been made that electrocardiographic evidence of severe myocardial hypoxia may develop in the absence of apparent mechanical constriction of the coronary circulation. In the presence of such myocardial hypoxia, decompensation of the right ventricle was observed and pulmonary hypertension was no longer maintained.

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INTRACARDIAC LEFT-TO-RIGHT SHUNT WITH PULMONIC STENOSIS

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RECENT success in surgical closure of auricular septal defect[1-3] has stimulated a renewed interest in the differential diagnosis and hemodynamics of left-to-right cardiac shunts. A number of cases of intracardiac left-to-right shunt associated with pulmonic stenosis were encountered during the course of cardiac catheterization studies. A review of the clinical, radiologic, and electrocardiographic data of these cases has suggested that the combination of these anomalies may be recognized clinically. The purpose of this report is to describe the clinical features and hemodynamics in ten cases of left-to-right shunt with pulmonic stenosis and to consider the advisability of surgery. A case presentation with autopsy findings is also included.

MATERIAL AND METHODS

The study includes ten children admitted to the Cardiology Division of the Children's Medical Center. A careful history was recorded and detailed physical examination carried out. Fluoroscopic and radiologic examinations were performed in every patient. Electrocardiograms were obtained in all, and phonocardiograms were taken in six cases.

Cardiac catheterization was performed under morphine and Nembutal sedation. Besides the usual blood samples obtained for diagnostic purposes, samples were procured simultaneously from the main pulmonary artery and the exposed brachial artery during the collection of a three-minute sample of expired air, for determination of cardiac output. (In two children, expired air was not obtained due to lack of cooperation.) Pressure measurements were made with a Sanborn electromanometer and recorded by a Sanborn Polyviso apparatus; the zero level was taken at 5 to 6 cm. anterior to the spine, depending on the anteroposterior chest diameter. The oxygen content and capacity of the blood samples collected were determined manometrically in the Van Slyke apparatus.

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*Research Fellow of the Webster-Underhill Fund.

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The oxygen content of the expired air was measured by means of a Pauling apparatus, and the expired air volume determined in a Tissot spirometer. In the two cases where oxygen consumption could not be measured, it was assumed as 180 c.c./M.^{2}/min. Pulmonary and systemic flows were estimated by the Fick principle.

Pulmonary valve resistance was measured from the mean systolic ejection pressure gradient between the right ventricle and pulmonary artery, and the pulmonary blood flow, utilizing Poiseuille's formula and expressed in dyne/sec./cm.$^{-5}$ Total pulmonary vascular resistance was similarly calculated from the gradient between mean pulmonary artery and pulmonary capillary-venous or left-atrial pressure. Pulmonary valve orifice size was estimated by the Gorlin formula.[3]

CLINICAL FEATURES

Ten patients were studied, seven females and three males. Six had a left-to-right shunt at the auricular level, three at the ventricular level, and one child had an ostium auriculoventriculare commune proved at autopsy.

There were no symptoms referable to the cardiac anomaly in any of these children. No history of cyanosis, exercise intolerance, congestive failure, or frequent respiratory infection was elicited.

Certain features of the physical examination of these children may be discussed without regard to the level of the left-to-right shunt. They were all of average height, but somewhat underweight according to the Children's Medical Center anthropometric chart. No cyanosis or clubbing was noted. The blood pressure was within normal limits. Chest deformity was noted in six patients. Cardiomegaly, or hyperactive cardiac impulse, and a precordial systolic thrill were present in all patients, and on auscultation, there was a harsh systolic murmur at the second left intercostal space, transmitted to the neck and back. Ventricular septal defect with pulmonic stenosis could be differentiated from atrial septal defect with pulmonic stenosis by the presence of an additional systolic murmur and thrill at the lower left sternal border.

Apical mid-diastolic murmurs were present in all but one patient. The pulmonic second sound was uniformly either of normal or diminished intensity and was more widely split in patients with atrial than in those with ventricular shunts.

Cardiac fluoroscopy and x-ray examination showed considerable cardiac enlargement with dominance of the right ventricle. Pulmonary vascular engorgement was uniformly present and was associated with expansile pulsation in six patients.

The electrocardiogram revealed incomplete right bundle branch block in every patient. The presence of right ventricular hypertrophy was also suggested by a tall secondary R wave in Lead V_1 in all.

The clinical picture described here represents a combination of some of the features of the individual lesions. Thus, the major diagnostic problem in cases of left-to-right shunt with pulmonic stenosis is to differentiate this syndrome from isolated pulmonic stenosis, atrial septal defect, or ventricular septal defect alone.

TABLE I. DIAGNOSIS OF AURICULAR SEPTAL DEFECT, PULMONIC STENOSIS, AND COMBINED LESIONS

	CARDIAC IMPULSE AT XIPHOID	THRILLS AT 2 LIS	SECOND HEART SOUND AT 2 LIS		MURMURS	X-RAY	ECG
			SPLITTING	INTENSITY			
Auricular septal defect (A.S.D.)	Hyperactive	0	Wide	Normal	Blowing systolic at 3 Lis. Middiastolic at apex	Moderate cardiomegaly. PV increased ± dance	Incomplete RBBB; ± RVH
Pulmonic stenosis (P.S.)	Not very active	+	Narrow	Decreased	Rough systolic at 2 Lis	Slight cardiomegaly. PV normal or decreased	RVH
A.S.D. and P.S.	Hyperactive	+	Wide	Decreased	Rough systolic at 2 Lis. Middiastolic at apex	Marked cardiomegaly. PV increased ± dance	Incomplete RBBB; + RVH

2 Lis = second left intercostal space; 3 Lis = third left intercostal space; PV = pulmonary vasculature; RBBB = right bundle branch block; RVH = right ventricular hypertrophy.

TABLE II. DIAGNOSIS OF VENTRICULAR SEPTAL DEFECT, PULMONIC STENOSIS, AND COMBINED LESIONS

	CARDIAC IMPULSE	THRILLS	SECOND HEART SOUND AT 2 LIS		MURMURS	X-RAY	ECG
			SPLITTING	INTENSITY			
Ventricular septal defect (V.S.D.)	Hyperactive	3 and 4 Lis	Normal	Loud	Rough systolic at 3 and 4 Lis. Middiastolic at apex	Moderate cardiomegaly. PV increased ± dance	LVD; ± RVH
Pulmonic stenosis (P.S.)	Not very active	2 and 3 Lis	Narrow	Decreased	Rough systolic at 2 Lis	Slight cardiomegaly. PV normal or decreased	RVH
V.S.D. and P.S.	Hyperactive	2-4 Lis	Normal	Decreased	Rough systolic 2-4 Lis. Middiastolic at apex	Marked cardiomegaly. PV increased ± dance	Incomplete RBBB; ± RVH

3 Lis = third left intercostal space; 4 Lis = fourth left intercostal space; PV = pulmonary vasculature; LVD = left ventricular dominance; RVH = right ventricular hypertrophy; 2 Lis = second left intercostal space; RBBB = right bundle branch block.

Table I attempts to present the significant features in the differentiation of auricular septal defect with pulmonic stenosis from the individual defects, and Table II presents the same information in relation to ventricular septal defect with pulmonic stenosis.

The phonocardiographic demonstration of the points in differential diagnosis is illustrated in Figs. 1 and 2, with a schematic presentation of the phonocardiogram above the tracing. Fig. 1 shows the diamond-shaped systolic murmur

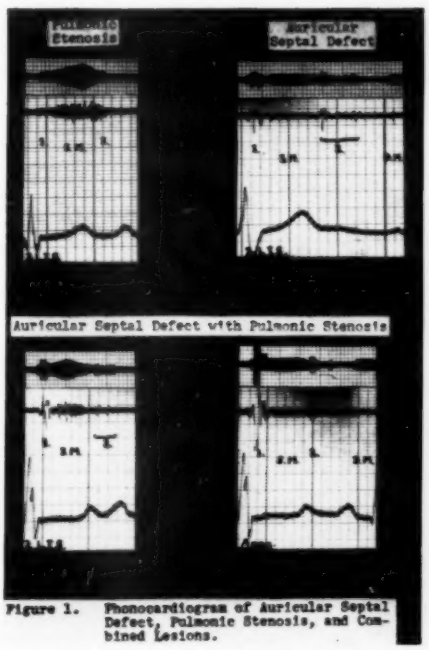

Figure 1. Phonocardiogram of Auricular Septal Defect, Pulmonic Stenosis, and Combined Lesions.

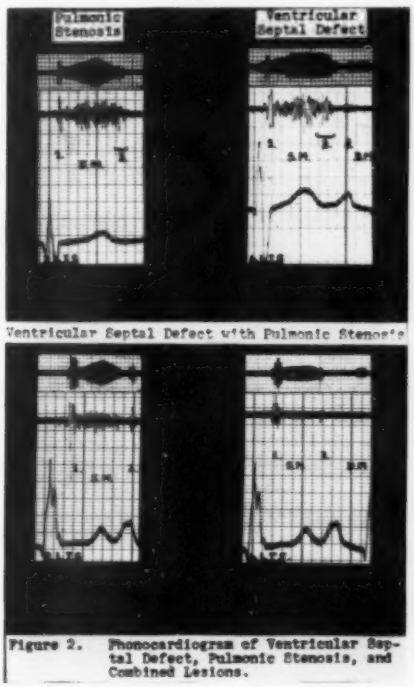

Figure 2. Phonocardiogram of Ventricular Septal Defect, Pulmonic Stenosis, and Combined Lesions.

Fig. 1.—Top line is schematic drawing of the phonocardiogram, middle line is actual phonocardiogram, bottom line is electrocardiogram, Lead II.

Fig. 2.—Arrangement the same as in Fig. 1.

with the low-amplitude and narrowly split second sound at the second left intercostal space found in atrial septal defect. The combination of pulmonic stenosis with left-to-right shunt through an atrial septal defect results in the features of pulmonic stenosis, with a mid-diastolic apical murmur. Similar features are demonstrated in Fig. 2, where left-to-right shunt through a ventricular septal defect is associated with pulmonic stenosis. Ventricular septal defect shows a plateau-shaped systolic murmur maximal at the fourth left intercostal space. A combination of the lesions results in the auscultatory phenomena of ventricular septal defect at the fourth left intercostal space, with those of pulmonic stenosis at the second left intercostal space, and a mid-diastolic apical murmur.

The following report demonstrates some of the essential clinical features described previously; this is the only patient in the series who has come to autopsy.

CASE REPORT

L. A., (Table III, No. 10) a 6-year-old girl, was known to have had a heart murmur since the age of 3 months. She developed normally except that she had always been rather thin. A pink discoloration of the fingers and toes had been noticed for 3 years. The rest of the history was noncontributory.

3 Lis = third left intercostal space; 4 Lis = ventricular hypertrophy; 2 Lis = second left intercostal space; RBBB = right bundle branch block.

Physical examination revealed the girl to be in the fiftieth percentile for height and the tenth percentile for weight. There was a bright pinkness of the fingers and toes, but no cyanosis. The liver was palpable just below the right costal margin. The left precordial region was prominent. The cardiac apex was in the midaxillary line, and there was a hyperactive heaving impulse maximal at the lower left sternal border. A systolic thrill was palpable along the whole left sternal border. The first heart sound was accentuated at the apex; the second sound was normally split and of average intensity at the second left intercostal space. A Grade 4 systolic murmur was present along the whole left sternal border; a Grade 3 apical mid-diastolic murmur and a Grade 3 early diastolic blow at the third left intercostal space were also noted.

X-rays and fluoroscopy of the chest revealed an enlarged heart, with predominance of the right ventricle. Increased pulmonary vasculature, without intrinsic pulsation, was present, and some auricular enlargement was demonstrated (Figs. 3 and 4). The electrocardiogram showed prolonged auriculoventricular conduction with incomplete right bundle branch block and tall secondary R waves in the right precordial leads.

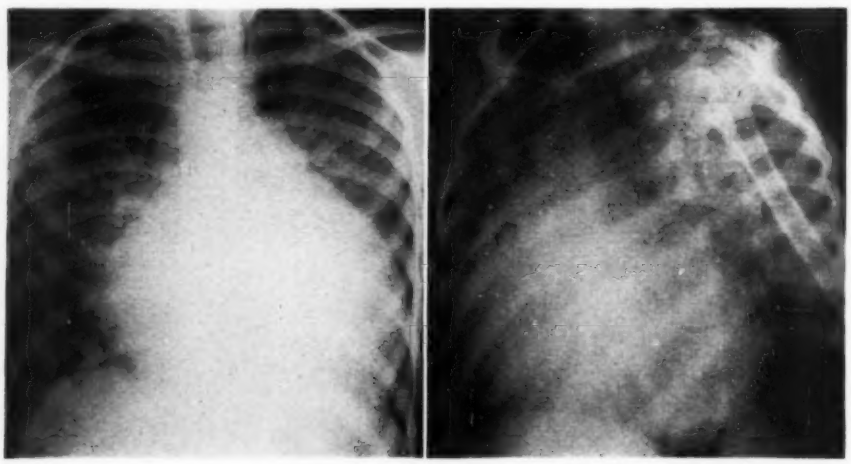

Fig. 3. Fig. 4.

Fig. 3.—Chest film. Anteroposterior view of Case 10.

Fig. 4.—Chest film. Left anterior oblique view of Case 10.

Cardiac catheterization supplied the following information:

	PRESSURE	OXYGEN CONTENT VOL. %	OXYGEN SATURATION (%)
Superior vena cava		10.76	63
Right auricle high		13.98	
Right auricle mid-lateral		15.65	
Right auricle mid	mean 5	14.80	
Right ventricle	62/5	15.23	
Main pulmonary artery	29/4 mean 17	15.05	
Right main pulmonary artery		15.24	
Pulmonary "capillary"	mean 9	16.88	98
Femoral artery	98/57 mean 68	15.81	92

Oxygen capacity—Sample 1, 17.06. Sample 10, 17.06.

Further information is given in Table III.

In view of the fairly large left-to-right shunt which appeared to be at the atrial level, and in view of the marked cardiomegaly, closure of an auricular septal defect was attempted by Dr. Robert E. Gross. Exploration through a rubber well attached to the right auricle revealed a huge auricular opening which seemed to be associated with an ostium auriculoventriculare commune. The auricular portion of the defect was closed by suturing a polyethylene sheet across the opening. However, soon after completion of the procedure, the child suddenly succumbed.

Autopsy examination of the heart showed a greatly enlarged right auricle and right ventricle. The right ventricular myocardium was thickened, measuring 0.4 to 0.7 cm.; the left ventricular myocardium measured 0.3 to 1.2 cm. in thickness. The pulmonary artery was markedly dilated. Measurements of the valves were as follows: pulmonic valve 6 cm. in circumference; mitral valve, 8 cm.; aortic valve, 4 cm.; the tricuspid valve was not opened but measured 4 x 2 cm. The foramen ovale was slightly patent. The pulmonic valve cusps were somewhat thicker than normal, but no stenosis was present. The posterior cusp of the mitral valve was thickened and shortened; it had no chordae tendineae attached to it, and it was fused with the edge of an interventricular septal defect. The posterior cusp of the tricuspid valve was also attached to the edge of the ventricular septal defect. The anterior cusps of the mitral and tricuspid valves were continuous. A ventricular defect 2.5 x 1.5 cm. in size extended upward into the lower part of the auricular septum, so that an atrioventriculare commune was present.

HEMODYNAMIC OBSERVATIONS

Table III summarizes the important information obtained in our ten cases.

Blood flows: Studies of the estimated blood flows revealed systemic flows within normal range in all cases. The pulmonary blood flows were larger than the respective systemic flows due to left-to-right shunting of blood. Pulmonary flows were increased from 1.2 to as much as 5.3 times the respective systemic flows.

Slight arterial unsaturation was present in three children (No. 4, 5, and 6). The catheter passed through an atrial defect in these three cases. The oxygen unsaturation noted in the left auricle indicated a small right-to-left shunt in addition to the left-to-right shunt at the auricular level.

Pressures: A significant mean systolic pressure gradient between the right ventricle and pulmonary artery was demonstrated in all cases ranging from 15 to 49 mm. Hg. The sudden drop in pressure and the site of this drop on slow withdrawal of the tip of the catheter suggested that the stenosis was valvular in all instances. The pulmonary pressures were in the normal range. The right ventricular systolic pressures were slightly to moderately elevated, but in all instances did not approach systemic systolic pressures. The combined pulmonary valve and pulmonary vascular resistance was always elevated, but never to the systemic level. The difference between systemic and total pulmonic resistance therefore resulted in a left-to-right shunt.

Reference to Table III reveals the expected correlations between the valve resistance from stenosis and the right ventricular pressure, pulmonary blood flow and amount of left-to-right shunt. Thus, the larger valves, with less resistance, allow for greater pulmonary flows at lower right ventricular pressures. The more stenotic valves are associated with higher right ventricular pressure and smaller left-to-right shunts and in some instances associated right-to-left shunt.

TABLE III

NO.	NAME	AGE (YR.)	SEX	B.S.A.	O_2 CONS. C.C./MIN.	O_2 SAT. (%)	O_2 CAP. VOL. (%)	FLOWS L./MIN.			PRESSURES (MM. HG)		RESISTANCES DYNE/SEC./CM.$^{-5}$			PULMONARY VALVE (CM.^{2})
								PULMONARY	SYSTEMIC	L TO R SHUNT	RIGHT VENTRICLE	PULMONARY ARTERY	MEAN SYSTOLIC GRADIENT	PULMONARY VASCULAR	PULMONARY VALVE	
A.S.D.																
1.	P.P.	5 8/12	F	0.7	138	98	15.82	11.5	4.2	7.3	36/0	18/6	15	67	70	1.84
2.	C.N.	7 0/12	F	0.8	110	96	15.91	5.0	2.2	2.8	39/1	14/4	22	65	232	0.82
3.	J.Z.	6 6/12	F	0.8	140	99	15.18	15.4	2.9	12.5	48/5	20/14	18	92	74	2.28
4.	V.W.	9 6/12	M	1.03	193	91	18.65	9.0	4.5	4.5	63/3	23/11	27	48	165	1.28
5.	J.L.	3 6/12	M	0.6	108*	92	15.27	6.0	3.2	2.8	57/2	18/8	30	73	226	0.89
6.	M.S.	3 6/12	M	0.7	137	91	16.93	5.5	4.6	0.9	62/0	17/9	29	115	388	0.55
V.S.D.																
7.	K.E.	5 5/12	F	0.8	162	99	16.91	16.2	6.4	9.8	39/0	24/6	16	70	65	2.5
8.	C.C.	3 1/12	F	0.48	82*	95	15.00	3.9	2.1	1.8	78/3	28/10	49	153	635	0.44
9.	J.L.	4 9/12	F	0.73	147	98	14.72	15.5	5.9	9.6	64/0	46/16	19	77	164	1.29
A-V Comm.																
10.	L.A.	6 0/12	F	0.72	145	91	17.06	8.4	2.9	5.5	62/5	29/4	33	104	230	1.02

L to R = left-to-right; A.S.D. = auricular septal defect; V.S.D. = ventricular septal defect; A-V Comm. = ostium auriculoventriculare commune; R to L = right-to-left; O_2 Cons. = oxygen consumption; Art. O_2 Sat. = arterial oxygen saturation; O_2 Cap. = oxygen capacity; B.S.A. = body surface area.

*Assumed.

DISCUSSION

The association of pulmonic stenosis with left-to-right shunt has been previously recorded by Abrahams,[15] Wood,[6] and by Broadbent and associates.[7] The diagnosis has been made on the basis of data obtained by cardiac catheterization. However, it may be possible to recognize this combination clinically, as indicated by the findings in the cases presented. The association of the characteristic rough systolic murmur of pulmonic stenosis at the upper left sternal border with features of a left-to-right shunt, as indicated by a hyperactive cardiac impulse, a mid-diastolic apical murmur and pulmonary plethora on x-ray, suggests the diagnosis.

The hemodynamic aspects of these cases are of considerable interest. Left-to-right shunting of blood is dependent on the higher resistance in the systemic as compared to the pulmonary arteriolar bed. A pulmonic stenosis of severe degree, with a valve resistance in the systemic range, does not allow for a left-to-right shunt through an associated defect and may be accompanied by a right-to-left shunt. The stenosis in our cases must thus necessarily be of mild or moderate degree. The magnitude of the left-to-right shunt will depend not only on the degree of stenosis, but also in some cases on the size of the associated defect. Some of these defects are probably too large to present an appreciable resistance to shunt flow, however, and therefore the dynamics of shunt are determined almost entirely by the relationship of pulmonary to systemic resistance.

In view of the absence of evidence of pulmonic stenosis in one child (Case 10, Table III), who succumbed during a surgical attempt to close the atrial opening, the problem has arisen whether or not the pulmonic stenosis is anatomic in these cases. An organic pulmonic stenosis could not be demonstrated in this case, and it was suggested that the stenosis was functional, relative to the increased pulmonary flow. However, much larger pulmonary flows have been encountered without any demonstrable pressure gradient across the pulmonary valve. One might postulate that in some individuals with left-to-right shunt and considerable cardiomegaly, there is a lack of dilatation of the pulmonary valve ring relative to the right ventricular outflow tract and the pulmonary artery, resulting in a mild functional stenosis. That this concept may be tenable is supported by our experience in another child subjected to surgery (No. 3). Closure of the atrial defect resulted in decreased cardiac activity, disappearance of the mid-diastolic murmur, decrease in heart size and, also, almost complete disappearance of the characteristic pulmonic stenosis murmur. It is unlikely that all the cases presented are of this nature. In the children with the larger pressure gradients across the pulmonary valve and with smaller left-to-right shunts it is probable that a true mild or moderate organic stenosis exists. It does not seem feasible that a small left-to-right shunt could result in sufficient dilation of the right ventricular outflow tract to produce a relative valvular stenosis.

The prognosis of this syndrome is not known. Most of these children have cardiomegaly, and it would appear that when the right ventricle is subjected to a combination of increased flow work at an increased pressure, it does not tolerate the burden very well. In view of the cardiomegaly, any procedure which could

decrease the work of the right ventricle would be advisable. A relief of the pulmonary stenosis would not seem desirable in view of the fact that it is not marked, and since any reduction of the resistance in the pulmonary circulation would increase the left-to-right shunt. However, elimination of the left-to-right shunt by closure of the defect would decrease pulmonary flow. Reduction of pulmonary flow may affect the pulmonic stenosis in two ways: (1) reduction of flow will be accompanied by a fall in gradient across the pulmonary valve. On the basis of Gorlin's formula, the flow is related to the square root of pressure; thus a reduction of flow by one-half will result in a four-fold decrease of the pressure gradient; (2) the right ventricular outflow tract and pulmonary artery may decrease in size and minimize any relative pulmonary valvular stenosis, if the concept of pulmonary valvular dilatation proves tenable.

In large left-to-right shunts, therefore, closure of the defect may be advisable, and the mild pulmonic stenosis should not deter surgical elimination of the shunt.

SUMMARY

1. The clinical features of ten children with left-to-right intracardiac shunt associated with moderate pulmonic stenosis are reviewed. Six had auricular defects, three ventricular defects, and one an ostium auriculoventriculare commune.

2. The relationship between the degree of stenosis, the right ventricular pressure, and the size of the left-to-right shunt is discussed.

3. The nature of the pulmonic stenosis is discussed. It is suggested that in some instances it is relative to enlargement of the right ventricle and pulmonary artery.

4. The surgical implications of the pulmonic stenosis and of the left-to-right shunt are considered.

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THE EFFECT OF BLOOD PRESSURE REDUCTION WITH ARFONAD* ON RENAL HEMODYNAMICS AND THE EXCRETION OF WATER AND ELECTROLYTES

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THE use of continuous infusions of ganglionic blocking agents has increased the applicability of controlled hypotension for use in some surgical procedures wherein profuse bleeding from small blood vessels may become a problem. If this procedure is to be used generally, it seems desirable that studies be made on the effect of blood pressure reduction on vital vascular beds such as the kidney. The current investigation is concerned with measurements of the renal hemodynamic response to blood pressure reduction with Arfonad,* one of the most potent ganglionic blocking agents,[1] which is used for controlled hypotension during surgery. In addition to renal hemodynamic studies, data were collected on glomerular filtration rate and on the excretion of water and electrolytes. Observations were also made on the effect of blood pressure elevation with norepinephrine on these responses.

METHODS

Renal function studies were carried out on nine unanesthetized normotensive subjects. Inulin was used to determine glomerular filtration rate (GFR) and para-aminohippurate (PAH) was used to estimate renal plasma flow (RPF). The mean blood pressure was determined by direct intra-arterial manometry and arterial blood samples for analyses were collected through a manifold. Analytical methods and techniques have been described previously.[2,3] All observations were made with the patient in the supine position. Sodium and potassium excretion rates were determined using a Beckman flame photometer for analysis.

After three successive ten-minute control periods, the Arfonad was administered by continuous infusion using a concentration of 2 to 4 mg. per c.c. of 5 per

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*Arfonad is *d*3,4-(1,3′-dibenzyl-2′-ketoimidazalido)-1,2-trimethylene thiophanium *d*-camphor sulfonate which was furnished by Hoffman-LaRoche, Inc.

TABLE IA. RENAL HEMODYNAMIC RESPONSE TO

PATIENT	MEAN BLOOD PRESSURE* MM.HG					RENAL BLOOD FLOW ML./MIN.					RENAL VASCULAR RESISTANCE†				
	C	D_1	D_2	D_3	D_4	C	D_1	D_2	D_3	D_4	C	D_1	D_2	D_3	D_4
1. C.E.	78	60	57	57	49	1594	847	1209	977	542	.05	.07	.05	.06	.09
2. C.S.	109	59	67	62	67	945	548	773	639	852	.12	.11	.09	.10	.08
3. R.V.	102	79	79	68	58	1551	743	798	542	311	.07	.11	.10	.13	.19
4. R.H.	90	88	73	59	60	—	—	—	—	—	—	—	—	—	—
5. J.M.	120	113	102	85	69	—	—	—	—	—	—	—	—	—	—
6. M.S.	111	101	81	67	50	675	521	257	487	123	.16	.19	.32	.14	.41
7. P.W.	106	94	85	73	65	1064	1200	1120	732	700	.10	.08	.08	.10	.09
8. J.S.	70	70	63	59	51	1155	745	903	950	512	.06	.09	.07	.06	.10
9. L.P.	98	69	72	58	41	1014	817	691	550	491	.10	.08	.10	.11	.08
Mean	98	81	75	65	57	1143	774	822	697	504	.09	.10	.12	.10	.15
Per cent of control		83	77	66	58		68	72	61	44		111	133	111	167
P value less than‡		.02	.01	.01	.01		.02	.02	.01	.01		NS	NS	NS	.30

*Direct arterial manometry

$$\text{†Renal Vascular Resistance} = \frac{\text{Mean Blood Pressure}}{\text{Renal Blood Flow}}$$

$$\text{‡}t = \bar{x}\sqrt{\frac{n(n-1)}{\Sigma x^2}}$$

C = Control
D_1 = First ten-minute period after blood pressure reduction with Arfonad
D_2 = Average of second and third ten-minute periods after blood pressure reduction with Arfonad
D_3 = Average of two ten-minute periods taken one hour after blood pressure reduction with Arfonad
D_4 = Average of two ten-minute periods taken two hours after blood pressure reduction with Arfonad

NS = $p > 0.30$

cent glucose in distilled water. The infusion rate varied between 2 and 6 c.c. per minute with an average of 3.5 c.c. The initial infusion rate was slow, but later in the study it was usually increased in order to obtain maximum reduction in blood pressure. If the initial rate of infusion was very rapid, a precipitous drop in blood pressure frequently occurred which was often associated with nausea and vomiting. If the blood pressure was reduced gradually over a ten to twenty minute period, the untoward side effects were both less frequent and much less severe. The infusion was continued with the patient remaining hypotensive for a 2 to 3 hour period. Observations were made on renal hemodynamics and on water and electrolyte excretion during the first thirty minutes of blood pressure reduction (three 10-minute periods), after one hour (two 10-minute periods) (D_3), and again after two hours (two 10-minute periods) (D_4). Then the blood pressure was increased to or above the control levels by an intravenous infusion

BLOOD PRESSURE REDUCTION WITH ARFONAD

HEMATOCRIT					PULSE RATE					BLOOD PRESSURE (AUSCULTATORY)									
										SYSTOLIC					DIASTOLIC				
C	D_1	D_2	D_3	D_4	C	D_1	D_2	D_3	D_4	C	D_1	D_2	D_3	D_4	C	D_1	D_2	D_3	D_4
47	45	43	44	45	82	86	86	86	85	108	82	81	78	70	60	56	56	50	50
36	35	34	33	37	88	80	60	72	78	150	82	90	84	93	100	55	62	60	62
43	42	41	40	38	70	74	78	82	82	130	104	100	84	70	80	78	70	56	40
46	45	46	46	46	64	70	84	68	72	112	114	96	82	90	68	68	58	54	50
26	25	25	24	24	98	104	100	96	100	144	142	128	98	90	96	82	78	52	50
43	42	40	39	40	82	88	96	88	84	130	118	94	82	68	94	84	70	54	48
42	41	41	40	40	70	80	72	72	62	134	120	110	84	70	90	70	68	58	46
40	40	41	40	40	78	112	112	100	96	102	110	88	84	88	64	60	56	54	40
42	42	42	40	43	80	80	78	84	76	100	90	80	74	54	84	60	60	50	38
41	40	39	38	39	79	86	85	83	82	123	107	96	83	77	82	68	64	54	47
	98	95	93	95		109	108	105	104		87	78	67	63		83	78	66	57
	.01	.20	.01	.02															

of norepinephrine and three successive 10-minute periods were collected (A_1 and A_2). During the norepinephrine infusion, observations were made on renal hemodynamics and on water and electrolyte excretion as was done during the hypotensive period.

RESULTS

A significant reduction in blood pressure ($p < 0.01$) was obtained in all of the patients to whom Arfonad was administered (Table IA). The maximum response for the group was obtained after two hours of drug administration at which time the drug was given at a maximum rate (average of 10 mg./minute for the group). The reduction in systolic pressure was about equal to the reduction in diastolic pressure. The reduction in blood pressure was usually associated with a sharp initial depression in renal blood flow which was even more marked after two hours of hypotension ($p < 0.01$). The renal vascular resistance increased slightly, although this change was not statistically significant ($p < 0.30$) even at the point of maximum depression in blood pressure and in renal blood flow. There was a tendency for the pulse rate to increase but this was not marked.

The reduction in renal blood flow (Table IA) was accompanied by a parallel reduction in glomerular filtration rate (Table IB) which was statistically significant at the 99 per cent level ($p < 0.01$).

Four out of nine patients vomited once or more during the study and two patients developed urticaria; a third developed generalized itching. These side reactions were not severe but tended to be more severe if the initial rate of infusion was very rapid.

TABLE IB. EFFECT OF BLOOD PRESSURE REDUCTION (WITH ARFONAD) ON GLOMERULAR FILTRATION RATE AND RENAL PLASMA FLOW

PATIENT	GLOMERULAR FILTRATION RATE ML./MIN.					RENAL PLASMA FLOW ML./MIN.					FILTRATION FRACTION					SIDE REACTIONS
	C	D_1	D_2	D_3	D_4	C	D_1	D_2	D_3	D_4	C	D_1	D_2	D_3	D_4	
1. C.E.	161	136	147	147	58	845	466	689	547	298	.19	.29	.21	.27	.19	Vomited (D_3), chills and rigors (D_4)
2. C.S.	137	57	81	74	97	605	356	510	428	537	.23	.16	.16	.17	.18	Dizzy when MBP below 58
3. R.V.	103	73	68	59	29	884	431	471	325	193	.12	.17	.14	.18	.15	Vomited (D_3), chills
4. R.H.	194	181	129	128	183	—	—	—	—	—	—	—	—	—	—	Generalized itching
5. J.M.	77	73	71	49	50	—	—	—	—	—	—	—	—	—	—	Vomited
6. M.S.	105	84	51	62	24	385	302	154	297	74	.27	.28	.33	.21	.32	Generalized itching, urticaria
7. P.W.	93	95	91	54	31	617	708	661	439	420	.15	.13	.14	.12	.07	Nausea, muscle tremor
8. J.S.	140	103	139	143	77	693	447	536	570	307	.20	.23	.26	.25	.25	Vomited, nasal stuffiness
9. L.P.	83	58	65	58	30	588	474	401	330	280	.14	.12	.16	.18	.11	Urticaria along infusing vein
Mean	121	96	94	86	64	660	455	489	419	301	.19	.20	.20	.20	.18	
Per cent of control		79	78	71	53		69	74	63	46		105	105	105	95	
P value less than		.30	.20	.10	.05		.05	.10	.01	.01		NS	NS	NS	NS	

C-D_4—See Table IA

$$\text{Filtration Fraction} = \frac{\text{Glomerular Filtration Rate}}{\text{Renal Plasma Flow}}$$

NS = $p > 0.30$

TABLE II. EFFECT OF BLOOD PRESSURE REDUCTION WITH ARFONAD ON WATER AND ELECTROLYTE EXCRETION

PATIENT	URINE VOLUME ML./MIN.					PLASMA SODIUM mEq./L.					PLASMA POTASSIUM mEq./L.					SODIUM EXCRETION μEq./min.					POTASSIUM EXCRETION μEq./min.				
	C	D_1	D_2	D_3	D_4	C	D_1	D_2	D_3	D_4	C	D_1	D_2	D_3	D_4	C	D_1	D_2	D_3	D_4	C	D_1	D_2	D_3	D_4
1. C.E.	0.7	0.6	0.3	0.7	0.1	137	137	137	140	140	4.46	4.46	4.17	4.17	4.17	74	57	23	20	7	40	28	27	30	26
2. C.S.	5.2	0.6	2.0	1.0	0.5	137	134	134	131	131	4.77	4.38	4.38	4.38	4.38	189	37	34	34	49	52	31	39	64	87
3. R.V.	7.3	8.6	1.3	0.5	0.4	137	135	138	137	137	3.74	3.74	3.43	3.46	3.46	103	91	41	27	15	26	17	29	31	21
4. R.H.	3.6	4.9	1.0	0.6	0.7	152	152	152	147	146	5.38	5.38	5.45	5.35	4.85	200	185	91	57	52	77	80	34	40	93
5. J.M.	6.7	6.4	5.2	4.2	3.3	146	149	147	147	146	4.41	4.07	3.87	3.89	3.58	473	410	396	286	234	197	178	188	132	150
6. M.S.	3.0	3.6	1.0	0.7	0.2	141	141	140	132	133	5.32	5.32	5.22	4.46	4.33	19	32	15	37	15	53	49	23	44	11
7. P.W.	0.7	0.8	0.8	0.3	0.6	146	144	144	140	141	5.03	4.92	4.62	4.20	3.92	120	137	85	33	16	19	22	36	34	29
8. J.S.	1.1	1.0	1.0	0.6	0.5	142	142	142	142	135	4.07	4.07	4.07	4.07	3.84	42	27	48	33	25	17	14	25	28	34
9. L.P.	6.5	2.4	0.9	0.7	0.4	141	141	141	138	131	4.12	4.10	3.92	4.10	3.79	225	63	90	65	21	25	25	36	37	24
Mean	3.9	3.2	1.5	1.0	0.7	142	142	142	139	138	4.59	4.49	4.35	4.23	4.04	161	115	91	66	48	56	49	49	49	53
Per cent of control		82	38	26	18		100	100	98	97		98	95	92	88		71	57	41	30		88	88	88	95
P value less than		NS	.02	.01	.01		NS	NS	NS	0.05		.30	.01	.02	.01		.10	0.01	.01	.01		.05	.20	NS	NS

C-D_4—See Table I for key to abbreviations
NS = $p > 0.30$

TABLE III. RENAL HEMODYNAMIC RESPONSE TO NOREPINEPHRINE WHEN THE BLOOD PRESSURE WAS PREVIOUSLY REDUCED WITH ARFONAD

PATIENT	MEAN BLOOD PRESSURE MM. HG.				RENAL PLASMA FLOW ML./MIN.*				GLOMERULAR FILTRATION RATE ML./MIN.				RENAL VASCULAR RESISTANCE†				RENAL BLOOD FLOW ML./MIN.				HEMATOCRIT			
	C	D_4	A_1	A_2	C	D_4	A_1	A_2	C	D_4	A_1	A_2	C	D_4	A_1	A_2	C	D_4	A_1	A_2	C	D_4	A_1	A_2
1. C.E.	78	49	71	88	845	298	404	806	161	58	104	156	.05	.09	.10	.06	1594	542	735	1465	47	45	45	45
2. C.S.	109	67	115	126	605	537	626	522	137	97	108	123	.12	.08	.12	.15	945	852	994	842	36	37	37	38
3. R.V.	102	58	101	123	884	193	458	360	103	29	53	59	.07	.19	.13	.20	1551	311	763	621	43	38	40	42
4. R.H.	90	60	102	96	—	—	—	—	194	183	177	180	—	—	—	—	—	—	—	—	46	46	46	46
5. J.M.	120	69	86	104	—	—	—	—	77	50	42	78	—	—	—	—	—	—	—	—	26	24	24	24
6. P.W.	106	65	102	141	617	420	675	437	93	31	72	80	.10	.09	.09	.19	1064	700	1125	728	42	40	40	40
7. J.S.	70	51	73	98	693	307	385	719	140	77	96	154	.06	.10	.11	.08	1155	512	642	1261	40	40	40	43
8. L.P.	98	41	85	125	588	280	338	181	83	30	58	54	.10	.08	.14	.37	1014	491	604	342	42	43	44	47
Mean	97	58	92	113	705	339	481	504	124	69	89	111	.08	.11	.12	.18	1221	568	811	877	40	39	40	41
Per cent of control		60	95	116		48	68	71		56	72	90		138	150	225		47	66	72		98	100	103
P value <		.01	NS	.05		.02	.10	.10		.01	.01	.10		NS	.05	.10		.02	.10	.10		NS	NS	NS
P value D_4‡ <			.01	.01			.02	.20			.05	.01			NS	.20			.02	.20			NS	NS

*Para-aminohippurate clearance

†Renal Vascular Resistance = $\frac{\text{Mean Blood Pressure}}{\text{Renal Blood Flow}}$

‡P Value using period D_4 (hypotensive period) for comparison rather than the control period prior to blood pressure reduction

C = Control observations (average of 3 ten-minute periods)

D_4 = Observations (average of 2 ten-minute periods) after blood pressure reduction for 2 hours

A_1 = First period after blood pressure elevation with norepinephrine

A_2 = Second and third 10-minute periods (average) after blood pressure elevation with norepinephrine

TABLE IV. EFFECT OF NOREPINEPHRINE ON WATER AND ELECTROLYTE EXCRETION IN PATIENTS PREVIOUSLY MADE HYPOTENSIVE WITH ARFONAD

PATIENT	URINE VOLUME ML./MIN.				PLASMA SODIUM mEq./L.				PLASMA POTASSIUM mEq./L.				SODIUM EXCRETION μEq./min.				POTASSIUM EXCRETION μEq./min.			
	C	D_4	A_1	A_2	C	D_4	A_1	A_2	C	D_4	A_1	A_2	C	D_4	A_1	A_2	C	D_4	A_1	A_2
1. C.E.	0.7	0.1	0.2	1.0	137	140	142	142	4.46	4.17	4.38	4.36	74	07	10	19	40	26	22	29
2. C.S.	5.2	0.5	1.5	2.7	137	131	136	133	4.77	4.38	4.33	4.35	189	49	74	93	52	87	118	118
3. R.V.	7.3	0.4	1.0	1.4	137	137	133	133	3.74	3.46	3.28	3.20	109	15	57	69	26	21	47	43
4. R.H.	3.6	0.7	1.0	0.7	152	146	147	148	5.38	4.85	3.46	3.46	200	50	42	68	77	79	90	91
5. J.M.	6.7	3.3	3.4	4.2	146	146	146	147	4.41	3.58	3.58	3.46	473	234	250	336	197	150	122	147
6. P.W.	0.7	0.6	1.3	1.6	146	141	144	144	5.03	3.92	3.92	3.92	120	16	85	122	19	29	59	53
7. J.S.	1.1	0.5	0.3	3.2	142	135	135	138	4.07	3.84	3.84	3.71	42	25	18	57	17	34	43	90
8. L.P.	6.5	0.4	3.2	1.6	141	131	131	134	4.12	3.79	3.79	3.33	225	21	101	75	25	24	55	43
Mean	4.0	0.8	1.5	2.1	142	138	139	140	4.50	4.00	3.82	3.72	179	52	80	105	57	56	70	77
Per cent of control		20	38	53		97	98	99		89	85	83		29	45	59		98	123	135
P value*		.01	.02	.10		0.05	0.20	0.20		.01	.02	.01		.01	.01	.02		.30	NS	.20
P value†			.10	.05			NS	NS			NS	.20			.05	.01			.20	.02

*This p value calculated using the control values prior to blood pressure reduction for comparison
†This p value is calculated using hypotensive period D_4 for comparison rather than the control period prior to blood pressure reduction
NS = $p > 0.30$
C = Control observations (average of 3 ten-minute periods)
D_4 = Observations (average of 2 ten-minute periods) after blood pressure reduction for 2 hours
A_1 = First period after blood pressure elevation with norepinephrine
A_2 = Second and third 10-minute periods (average) after blood pressure elevation with norepinephrine

The reduction in glomerular filtration rate was associated with concurrent reductions in water excretion ($p<0.01$, period D_4) and sodium excretion ($p<0.01$). These excretion rates (Table II) remained depressed throughout the entire hypotensive period and did not show any tendency to return toward the control levels. In fact, they actually decreased more as the blood pressure and glomerular filtration rate were reduced further. Initially potassium excretion was depressed significantly.

When norepinephrine was administered to eight of the patients, the blood pressure quickly returned toward or above the control levels. This was associated with a concurrent increase in glomerular filtration rate, which frequently did not return to the control value. Renal blood flow also increased ($p<0.02$), but did not return entirely to the control value. There was no statistically significant difference in the observations made during the first (A_1) and second (A_2) periods of norepinephrine infusion. Renal blood flow tended to remain depressed ($p<0.10$, period A_1). When the first period (A_1) during the infusion of norepinephrine was compared to the control values (C) before the blood pressure was reduced with Arfonad.

As the glomerular filtration rate increased following norepinephrine infusion, there was a concurrent increase in water excretion ($p<0.01$, period A_2) but this response was incomplete. The sodium excretion usually increased as the blood pressure rose but did not return to control values. Contrariwise, potassium excretion actually exceeded the control levels in many instances.

DISCUSSION

The tendency for Arfonad to produce a greater depression of renal function than hexamethonium[4] is probably due to the greater degree of blood pressure reduction with the former agent. This response should be anticipated since critical levels of blood pressure are being approached beyond which the intrarenal pressure is inadequate to maintain filtration through the glomerular membrane.[5,6] When the pressure is reduced below this critical level, glomerular filtration drops off rapidly.[6] The current data would indicate that renal blood flow is depressed at about the same blood pressure range that glomerular filtration is, probably due to inadequate hydrostatic pressure to force the blood through the renal blood vessels. However, the amount of blood which continued to flow through the kidney, at blood pressures herewith obtained, should be adequate to deliver sufficient oxygen to the renal tissue in order to prevent anoxia.

The reduction in water and electrolyte excretion is probably a reflection of the reduction in glomerular filtration rate without concurrent impairment of tubular reabsorptive mechanisms.[6] As a result, the percentage of filtered water and sodium that was reabsorbed was greater but the absolute amount was probably less. This would seem to be a point worth noting if intravenous fluids are to be administered in large amounts during surgical procedures which require controlled hypotension.

The ability of norepinephrine infusion to reverse these alterations of renal function indicate that the response in the first place is due to the blood pressure

reduction rather than being related to the Arfonad administration per se or to ganglionic blockade. The Arfonad was administered just as rapidly during the period of norepinephrine infusion as it was previously and, therefore, the same degree of ganglionic blockade must have been retained.

The degree of blood pressure reduction that can be obtained with Arfonad is considerably greater than that which is obtainable with other ganglionic blocking agents, such as hexamethonium and Pendiomide.* This probably accounts for the sustained depression in renal blood flow that occurs when maximum reduction in blood pressure is obtained with Arfonad as compared to hexamethonium.[4] No doubt the increased hypotensive effectiveness also accounts for the greater reduction in glomerular filtration rate with Arfonad than is seen with hexamethonium and Pendiomide.

SUMMARY AND CONCLUSIONS

1. Arfonad was administered by continuous intravenous infusion to nine normotensive individuals. After two hours of hypotension, norepinephrine was administered to eight of the patients. Observations were made on renal hemodynamics and on the excretion rates of water and electrolytes.

2. As the blood pressure was reduced, glomerular filtration rate and water and sodium excretion were depressed and remained so during the entire period of hypotension. Renal blood flow was likewise depressed and it did not compensate as has previously been observed with hexamethonium.

3. Norepinephrine administration returned renal function towards normal despite the continued infusion of Arfonad. Therefore, the depression of renal function during Arfonad administration is probably a reflection of the marked reduction in blood pressure that can be obtained with this agent rather than being related directly to the Arfonad.

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*pentamethyl-diethyl-3-aza-pentane-1,5-diammonium-dibromide, Ciba Pharmaceutical Products, Inc., Summit, N. J.

CLINICAL CALIBRATION IN PHONOCARDIOGRAPHY

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THE problem of "calibration" of heart sounds and murmurs has been a stumbling block which prevented clinical developments of phonocardiography for several decades. While a clinical tracing may be studied without reference to the absolute magnitude of sounds or murmurs, accurate determination of the latter is of interest and adds to the scientific accuracy of the method.

PREVIOUS STUDIES

A sound calibrator was devised by Olson and Massa. It was modified by Stodel and by Dunn and Rahm,[1] who based their device on comparison of two juxtaposed cathode-ray beams. A second type of calibrator (pistonphone), designed by the same authors,[2] provides an independent and absolute source of calibration. Both systems were used for calibration of microphones and not for direct calibration of the vibrations recorded from patients. The same applies to the calibrator of Mannheimer.[6]

Another type of calibrator was introduced by the Sanborn Company of Cambridge, Mass., in a recent model of their clinical phonocardiograph (Twinbeam). Its principle, briefly described by Wells and associates,[3] is the following: the compression of a button gives an electrical signal; this corresponds to a period of 60 vibrations per second and is recorded with a magnitude which is comparable to that of a sound of 90 decibels taking place within the microphone. This signal, having a low-pitched type of vibration, is attenuated by the filter used in "logarithmic" phonocardiography (Fig. 1).

The two systems described here have a certain value because they permit the use of a standard degree of amplification. When two tracings are recorded with the same magnitude of calibrating signal, instrumental differences can be excluded. On the other hand, several variables which can greatly modify the magnitude of the recorded vibrations are still present. They can be summarized as follows:

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(a) Changes due to different thickness of the air cushion (lung tissue) interposed between heart and chest wall. This may easily vary on account of a different phase of apnea and may further vary on account of pathologic changes of the lungs (emphysema, sclerosis), the pleura (fibrosis, effusion) or the pericardium (fibrosis, effusion).

(b) Changes due to different thickness of the chest wall and its surrounding tissues. This is particularly important if the microphone is even slightly displaced from its initial position, and particularly so in females (left breast).

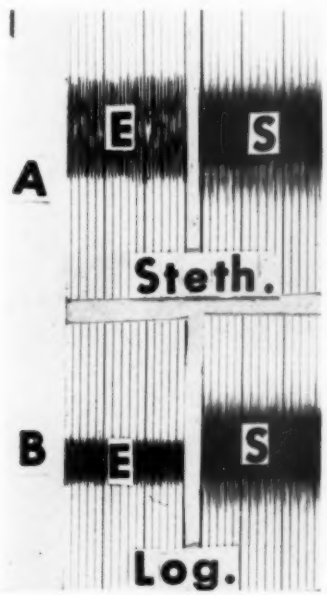

Fig. 1.—Stethoscopic (*A*) and logarithmic (*B*) registration of the Sanborn electric signal (*E*) and of the sound signal (*S*). Vibrator placed on a table at 10 cm. from the microphone.

(c) Changes due to different pressure of the air contained in the bell of a microphone on account of different tension of the rubber strap or, to a lesser extent, of the addition of a side chamber[4] (recording of both a "stethoscopic" and a "linear" tracing from the same bell).

It can be concluded that existing calibrators are useful for evaluating the degree of electrical amplification and the degree of weakening introduced by filters but not for clinical comparison.

TECHNIQUE

A new device was built.* This consisted of a 6-volt vibrator giving a sound signal of 100 cycles per second. It was connected with a battery, a switch, and a rheostat. The vibrator was enclosed in a 2 x 2 inch plastic box to be applied over the chest of the patient.

*This device was made by Mr. O. Fried, E.E., of the Allied Radio Corp., Chicago, Ill.

Loudness of the Signal.—The vibrator was placed on a table at 10 cm. distance from the open bell of a Sanborn microphone. The rheostat was adjusted so that the sound signal had the same amplitude as the electric signal of the Sanborn twin-beam through a "stethoscopic" registration.* As our device had a higher period than the Sanborn signal, it was altered to a lesser extent by "logarithmic" registration (Fig. 1).

OBSERVATIONS

1. *Placement of the Calibrator.*—The calibrator can be placed over any point of the chest. In several experiments in normal subjects, the results obtained with the device placed over the right chest, left chest, manubrium, trachea, or back, were compared. A special vibrator was also tried inside the mouth. The best position, found by trial and error, was over the rim of the left pectoral muscle, half-way between the axilla and the nipple (Fig. 2).

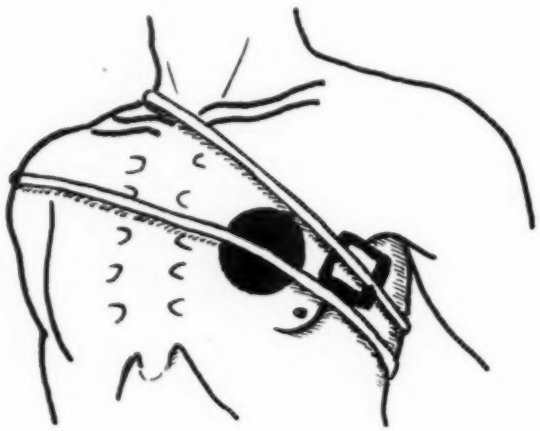

Fig. 2.—Best placement of the sound vibrator.

2. *Average Results.*—With the subject in a position of moderate inspiratory apnea and recording "stethoscopic" tracings, the following data can be obtained (Fig. 3): The sound signal is recorded at the apex with a magnitude comparable to that of the electric signal; it is recorded over the midprecordium from two to three times louder and is variably recorded over the aortic area from about two-thirds to one and one-half times as loud as the electric signal. On account of better transmission through the filter of the "logarithmic" system, sound signals are relatively louder than electric signals in "logarithmic" tracings.

3. *Effect of Interposed Layers.*—This was tried in two ways: (a) by interposing a wad of cotton between the skin and the bell of the microphone; and (b) by placing the latter above or below the left breast in females (Fig. 4). In both cases, the magnitude of the heart sounds sharply decreased and the magnitude of the sound signal also proportionally decreased.

*The terms "stethoscopic" and "logarithmic" are used in the sense meant by Rappaport and Sprague.[4] Additional technical details can be found in a recent publication of the author.[5]

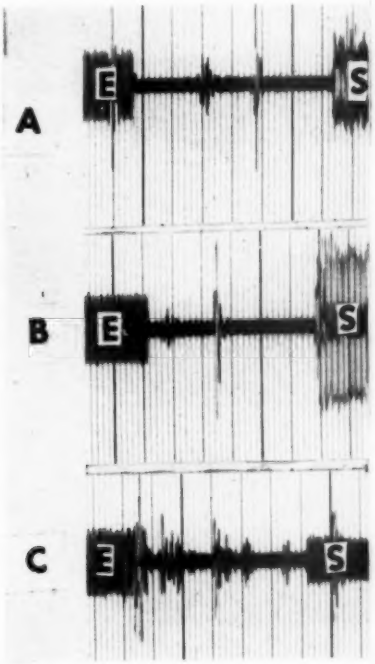

Fig. 3.—Calibration of heart sounds in a normal subject. *A*, Microphone at apex; *B*, Microphone at midprecordium; *C*, Microphone at aortic area. *E* = electric signal; *S* = sound calibrator over left pectoral muscle in all three tests.

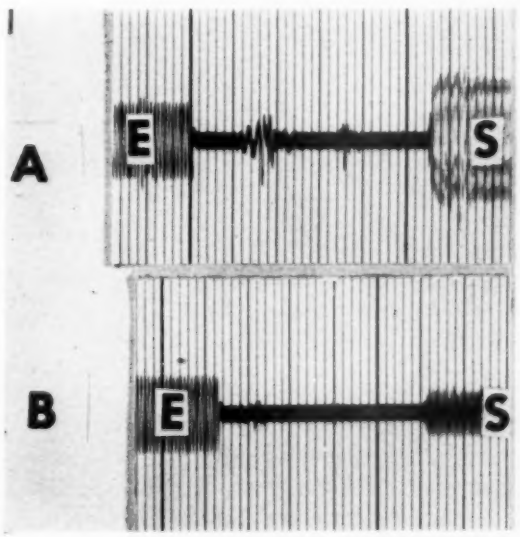

Fig. 4.—Calibration of heart sounds in a woman. In (*A*) the microphone is below the left breast; in (*B*) it is above breast. Striking decrease of magnitude of the sounds. Sharp decrease of vibrations of the sound calibrator.

4. *Slight Changes in the Position of the Microphone.*—Even a slight change in the angle of application of a microphone over the skin changed the magnitude of the heart sounds. The vibrations of the sound signal varied in the same direction of the heart sounds even though the changes were smaller (Fig. 5).

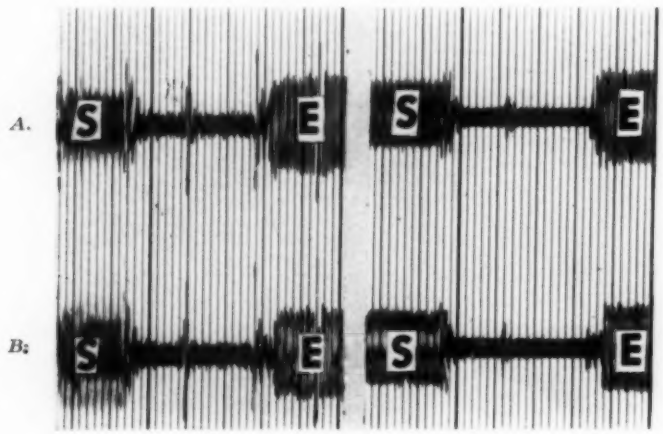

Fig. 5.—A slight change of position of the microphone may cause a sharp drop of intensity of the heart sounds. There is some drop of magnitude of the vibrations of the sound calibrator (*S*) while the electric signal (*E*) is unchanged. *A*, Stethoscopic tracings; *B*, logarithmic tracings. Simultaneous tracings from the same microphone.

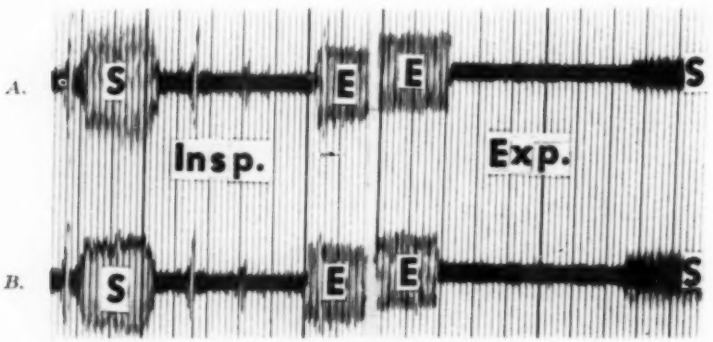

Fig. 6.—Sharp drop of magnitude of heart sounds from moderate inspiratory apnea to moderate expiratory apnea. The vibrations of the sound calibrator decrease in the same direction as the heart sounds. Symbols as in previous illustrations. *A*, Stethoscopic tracings; *B*, Logarithmic tracings. Simultaneous phonocardiograms from the same microphone.

5. *Respiration.*—Inspiratory and expiratory apnea modify the magnitude of the heart sounds. In general, with a predominantly abdominal respiration, expiratory apnea reduces the magnitude of the heart sounds; with a predominantly thoracic type of respiration, the heart sounds may decrease in inspiration. The vibrations of the sound signal decreased like those of the heart sounds, especially in the abdominal type of respiration (Fig. 6). In the forced inspiratory or expiratory apnea, on the contrary, the vibrations of the sound signal occasionally varied in the opposite sense of the heart sounds.

6. *Different Tension of the Rubber Strap Holding the Microphone.*—When the strap was placed under greater tension, the pressure of the air contained within the bell was increased, so that the skin acted as a tense membrane.[4] The amplitude of the heart sounds (and especially that of their low-pitched vibrations) was reduced. The vibrations of the sound vibrator was also reduced (Fig. 7).

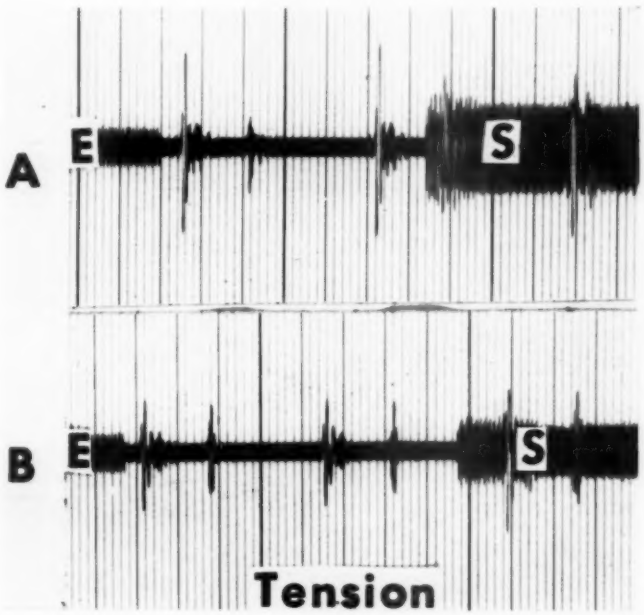

Fig. 7.—Drop of intensity of heart sounds obtained by increasing the tension of the rubber strap (*B*). The vibrations of the sound calibrator also decrease.

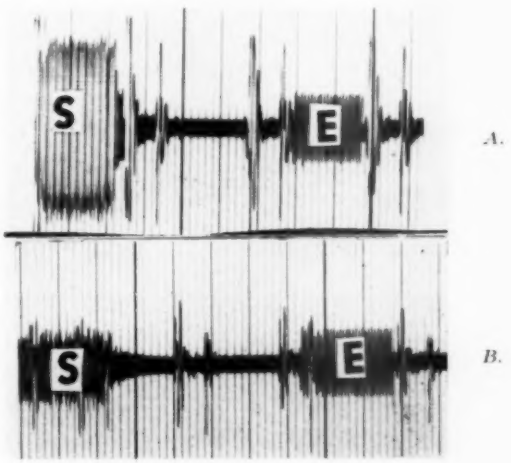

Fig. 8.—Experimental production of pleural effusion in a dog. *A*, Stethoscopic tracing of the apex before intervention. *B*, Same tracing after injection of fluid into the left pleural cavity. The vibrations of the sound calibrator decrease more than those of the heart sounds.

7. *Presence of Fluid or Air in the Pleural Cavities.*—Fluid was introduced in the left pleural cavities of two dogs. The magnitude of both the heart sounds and the vibrations of the sound calibrator were greatly reduced (Fig. 8). On the contrary, pneumothorax, also tried in two dogs, increased the loudness of the signal while it reduced (one experiment) or left unchanged (one experiment) the heart sounds.

DISCUSSION

If the vibrations of the sound signal could be made to arise within the mediastinum, their transmission would be modified by the same causes which modify the transmission of the heart sounds. All efforts in that direction having failed, the sound calibrator was applied over the chest wall and the best location was empirically established.

With the calibrator over the left pectoral muscle (Fig. 2), the vibrations seem to be transmitted partly through the chest wall and partly through the lungs. This was demonstrated by animal experiments and was confirmed by various observations in man.

Various causes of error of phonocardiography, like changes of the electrical characteristics of the system, modification of tension of the microphone against the skin, variable thickness of the chest wall, or improper application of the microphone, are automatically revealed by changes in magnitude of the vibrations of the sound calibrator, so that the latter may be effectively used as a standard.

Changes of resonance of the chest wall due to pleural effusion are fairly well revealed by the calibrator, even though no absolute proportion can be found between the changes of magnitude of the heart sounds and those of the vibrations of the signal. On the other hand, less accurate proportionality was found in dealing with respiratory variations. This applied particularly to extreme inspiratory or expiratory apnea. Several experiments revealed the interaction of multiple factors: (a) displacement of the heart within the chest; (b) changes of magnitude of one or both heart sounds due to changes of venous return; and (c) changes of transmission due to greater or lesser interposition of the lungs between heart and chest wall. It is apparent that only a signal arising within the heart could avoid all possible causes of error. On the other hand, avoidance of the extreme respiratory positions and recording of the heart sounds in intermediate apnea avoids several causes of error and increases the value of the calibrator.

The sound calibrator should not be considered as a standard whose variations are absolutely proportional to those of the heart sounds. However, both vary usually in the same sense. A more exact proportionality can be demonstrated, on the other hand, for changes dealing with the application and location of the microphone and with changes of the chest wall.

In conclusion, even though the new device is far from perfect, it represents a definite step forward and may insure at least a gross comparison of clinical and experimental tracings.

USE OF THE SOUND CALIBRATOR

Calibration can be done in two ways: (a) by always using a certain magnitude of signal and recording the phonocardiogram at that degree of amplication; or (b) by selecting the best amplification for recording clearly recognizable sounds and murmurs, and including both the electric and the sound signal in the record (Fig. 9). The second method should be preferred because the first may yield tracings with either inadequate or excessive amplification.

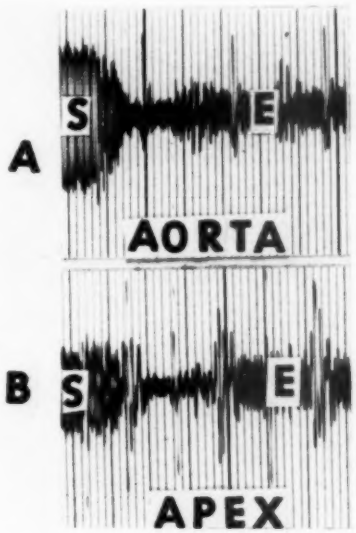

Fig. 9.—Calibration in a clinical case. *A*, Aortic area, louder sound calibration. *B*, Apex, sound calibration less loud, in spite of slightly increased amplification revealed by the electric calibration.

SUMMARY

1. The need for a sound calibration with a signal which varies in accordance with the manifold causes of error of clinical phonocardiography is emphasized.

2. A new, simple device is described. It is based on the production of a sound vibration of known amplitude and frequency over the chest wall and its transmission to the microphone.

3. The best location for placing the calibrator is described.

4. The transmission of the signal to various areas of the precordium is studied.

5. The variations of the signal in the various possible changes of the microphone, its location and application, are studied. Animal experiments offer opportunity to study the changes of the signal following experimental production of either pneumothorax or pulmonary effusion.

6. The advantages and disadvantages of the method are discussed.

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SONVELOGRAPHIC RECORDING OF MURMURS DURING ACUTE MYOCARDITIS

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IN any large group of patients with rheumatic valvular heart disease, only about one-half have a definite history of acute rheumatic fever. In the others the specific illnesses which produced inflammatory processes in the valves must have been overlooked. Until recently, failure to recognize acute attacks of rheumatic fever did not materially influence the course of the disease because subsequent attacks could not be prevented. Now that prophylaxis against recurrent episodes of rheumatic fever seems to be available, the necessity for accurate diagnosis becomes greater. Clinicians are now faced with the obligation of improving their diagnostic techniques to discover acute rheumatic fever as early as possible among the large group of patients which is currently escaping detection. In all probability these patients fail to exhibit the classical signs and symptoms currently accepted as criteria for the disease. Many of them undoubtedly display nothing more than a febrile illness attended by altered electrocardiographic patterns and possibly by transient heart murmurs. However, similar electrocardiographic signs occur with "acute nonspecific myocarditis," which is associated with a vast number of febrile illnesses and presumably is not responsible for chronic lesions of the valves and chordae tendineae. If this is true, such patients should be spared the psychologic, social, and economic complications of both incorrectly diagnosed rheumatic fever and prolonged prophylactic administration of antibiotics.

Diastolic murmurs simulating those produced by organic mitral stenosis are known to occur during attacks of acute rheumatic fever and to disappear during recovery.[1] It seems reasonable that patients exhibiting such murmurs might be more prone to develop chronic valvular damage. Many such murmurs represent relatively low-frequency vibrations which are frequently inaudible to some observers. In one sense the sounds produced by the heart can be compared to an iceberg since only part of the vibrations are perceptible. A large proportion of the low-frequency vibrations have relatively high intensity but are completely inaudible because the human auditory mechanism is notably insensitive to low-pitched sounds.[2,3] Theoretically, graphic records of the heart sounds should

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facilitate the detection and timing of such murmurs.[4] However, stethography has never played a prominent role in routine diagnosis despite the development of highly efficient audio amplifiers with sensitivities well beyond that of the human ear. Perhaps this is due to the fact that the quantity of useful information obtained by stethography is not commensurate with the time and expense involved in the photographic recording of heart sounds. The advent of direct-writing electrocardiographs threatens to eliminate stethography from the diagnostic armamentarium because the low-frequency galvanometers are incapable of accurately registering most sounds and murmurs. For this reason, heart-sound recording equipment has been developed for use with direct-writing instruments.[5] This particular form of heart-sound recording has been termed "sonvelography" to distinguish it from the more familiar types of stethographs or phonocardiographs.

METHODS

The Characteristics of the Sonvelograph.—A microphone, placed on the precordium, responds to sound vibrations by emitting a fluctuating electrical voltage which is amplified and recorded as the standard type of stethogram. The amplitude of these fluctuations is related to the intensity of the sounds while the frequency is indicated by the interval between the peaks of the deflections. High-frequency galvanometers are required to record these vibrations faithfully. On the other hand, a continuous line, connecting the peaks of the deflections, describes an "envelope" of the sounds which can be recorded by low-frequency galvanometers. The sonvelograph transforms the heart sounds into an "envelope" proportional to the logarithm of sound intensity (son = sound, velo = to envelope) but does not indicate the sound frequency. The derivation of the sonvelogram from the signal emitted by a microphone is indicated in Fig. 1,*A*. First, the signal is rectified so that all deflections have the same polarity. A filtering circuit of approximately 0.03 second time constant prevents the galvanometer returning to the base line between deflections, thus producing an envelope of the sound. The frequency and intensity response of the system simulates the characteristics of the human auditory apparatus.

The sonvelograph was designed to produce a record which would resemble the schematic drawing commonly used to illustrate the intensity and timing of murmurs in relation to the heart sounds. Although it is impossible to produce a sound recording system which precisely duplicates all the characteristics of human audition, a fair approximation can be achieved in the range of heart sounds by a logarithmic amplifier with a frequency response of the type illustrated in Fig. 1,*B*.

The Frequency Response.—When one listens to pure tones of equal intensity but with frequencies varying from 30 to 1,000 c.p.s., the low-pitched tones are barely audible but the high-pitched sounds seem very loud. Thus, the sensitivity of the auditory mechanism is maximal in the speech range, which is near 1,000 c.p.s., and is greatly reduced at lower frequencies. The sonvelograph in current use has a frequency response which simulates the hearing curve up to 200 c.p.s. and then levels off to reduce artifacts from extraneous noises, particularly breath sounds, because this equipment is frequently used on very young children whose

cooperation in breath holding is not always ideal. An amplifier with a frequency response conforming to an average hearing curve can be easily constructed.

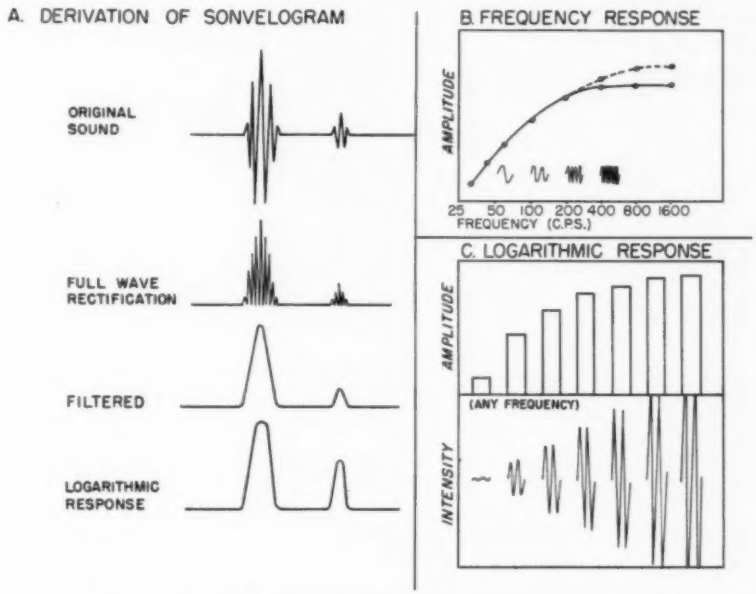

Fig. 1.—*A*, An envelope of sound vibrations is produced by rectifying and filtering the original signal so that the sound intensity is recorded as a continuous line which in effect would connect the peaks of the individual deflections. *B*, The amplitude of the deflections varies with the frequency of sound vibrations even though their intensity is constant. The frequency response of the amplifier (solid line) simulates the curve of human audition at low levels of intensity (interrupted line) up to 200 c.p.s. *C*, The response of the sonvelographic system is proportional to the logarithm of the sound intensity at any particular frequency.

The Logarithmic Response to Sound Intensity.—The human ear is capable of responding to a tremendous range of sound energies; a painful sound has some 10,000,000 times more energy than a sound at the threshold of audibility. This broad scale of sound intensities can be perceived because the "loudness" of a sound is related to the logarithm of the sound intensity. A similar logarithmic response of the sonvelographic amplifier is illustrated in Fig. 1,*C*. If the sound intensity is increased by equal increments, the amplitude of the response increases by progressively smaller amounts. In the lowest record of Fig. 1,*A*, the second sound produces a deflection more nearly equal to the first sound due to the combined effects of the logarithmic and frequency characteristics of the amplifier. The first and second heart sounds may appear to have similar loudness when the second sound has a higher frequency and lower sound energy than the first sound. The intensity response of the human ear varies somewhat with the frequency, a characteristic which cannot be easily duplicated with an amplifier.

Recording and Timing of Sonvelograms.—Sonvelographic records of heart sounds and murmurs have been recorded simultaneously with routine electrocardiograms using a Sanborn Twin-Viso. The patients are routinely relaxed in the supine position to avoid artifacts on the electrocardiograms. With few

exceptions, sounds and murmurs are also clearly elicited in this position. A Maico heart-sound microphone was placed successively in the following positions: (1) over the apical impulse, (2) at the third intercostal space at the left parasternal line, (3) at the second intercostal space at the left parasternal line, and (4) at the second intercostal space at the right parasternal line. Electrocardiographic tracings were recorded simultaneously from the three standard limb leads and aV_R, respectively. Even though the temporal relations between the electrical activity and the sequence of contraction are variable, electrocardiograms have been used for timing purposes for several practical reasons: (a) electrocardiography is the principal reason for referral of the patients, (b) sonvelograms can be rapidly and efficiently recorded in the course of routine electrocardiography, and (c) the additional time required to record arterial or venous pulses could not be spared. The first sound regularly begins just after the onset of the QRS complex, usually following the peak of the major deflection. The relation between the second heart sound and the T wave is not reliable for timing purposes. However, on at least one of the four records, the second sound is unmistakably identified and from such a record the temporal relation of the second sound to the first sound and to the electrocardiographic patterns in other tracings can usually be established with ease.

Advantages and Limitations of Sonvelographic Recording.—Reliable records of heart sounds can be obtained from low-frequency galvanometers only by some sort of compromise, which in this case involved a sacrifice of information regarding the frequency of the sounds. Clearly this method is not intended as an improvement on the more familiar stethographs which employ high-frequency galvanometers to indicate both the frequency and intensity of sounds. Indeed, the term sonvelograph was applied to this instrument to distinguish it from standard stethocardiographs. Nevertheless, sonvelography was found to compare favorably with auscultation and with recordings from a Sanborn Stethocardiette in the detection of heart murmurs in a controlled study.[6] During the past three years, it has also proved to be a convenient method for obtaining routine records of heart sounds and murmurs in the electrocardiographic laboratory of the Children's Orthopedic Hospital, Seattle, Washington.

The sonvelograph has the inherent advantages of any direct-writing instrument; the finished record can be inspected as it is written and no photographic processing is required. Permanent records of heart sounds can be obtained almost as quickly as the routine electrocardiogram, which is taken simultaneously. The patterns are simple and can be rapidly interpreted and compared. The sensitivity of the apparatus can be increased beyond the range of human auditory perception.

Sonvelography has limitations common to all forms of stethography. No inscribed record of sounds can substitute for auscultation in interpretation of heart sounds or murmurs. Many commonplace experiences indicate the features of human auditory perception which cannot be duplicated from sound vibrations recorded by a galvanometer. For example, sound waves from a single musical instrument can be selectively perceived from the tremendous number of vibrations produced by an orchestra, and a familiar voice can be instantly recognized over

the telephone. Neither of these feats could be accomplished by visual reference to recorded deflections. Thus, stethographic recordings are more appropriately used as guides to auscultation or for confirmation of subjective impressions. In this role sonvelography can be useful in spite of the fact that it provides no indication of the frequency of the sounds. For example, a deflection immediately following the second heart sound could be due to a third heart sound, opening snap of mitral stenosis or an early diastolic murmur. The identity and significance of such vibrations are preferably determined by auscultation. If the vibrations responsible for the deflections in early diastole cannot be heard, their significance is in doubt and they are regularly reported as "early diastolic sounds or vibrations which may be third heart sounds." Similarly, presystolic deflections are reported as "auricular sounds" unless they correspond to an audible murmur. Conservative interpretation of deflections which cannot be confirmed by auscultation is essential until criteria have been established for the significance of inaudible vibrations emitted by the heart.

RESULTS

Sample records illustrating the sonvelographic patterns produced by various heart sounds and murmurs are illustrated in Fig. 2. In the vertical column of records on the left, the top record reveals the first and second heart sounds without evidence of vibrations during either the systolic or diastolic intervals. The second record on the left illustrates a soft systolic murmur. The third record indicates a loud coarse systolic murmur as recorded from the pulmonary area of a patient with an atrial septal defect.

The remainder of the records in Fig. 2 illustrate heart-sound patterns obtained from patients with acute rheumatic carditis. A third heart sound produces a deflection on the descending limb of the second heart sound (top row, middle record) or very shortly after its termination as in the record in the upper right hand corner. Many normal children have audible third heart sounds but if this sound makes its appearance in the course of acute myocarditis, the resulting triple sound is classified as a gallop rhythm. Virtually all patients with acute rheumatic fever develop early diastolic deflections on serial sonvelograms taken in the course of the active process. These deflections apparently correspond to the vibrations described by Taquini and associates.[7] The transition from the typical third heart sound to the definite early diastolic murmur is illustrated in the center column of records in Fig. 2. No early diastolic vibrations were audible in the patient from whom the middle record was taken in spite of the large deflection on the sonvelographic record.

Deflections which immediately precede both the first sound and the initial deflection of the QRS complex are presumably auricular in origin; sometimes labeled as the fourth heart sound. In the upper right-hand record appears a definite presystolic deflection which in this case was inaudible. The record just below illustrates a much larger presystolic deflection which was also inaudible. These deflections superficially resemble the vibrations described by Alimurung and associates[8] but appear to precede the QRS complex. The lower right-hand

record illustrates a late diastolic (presystolic) murmur along with a systolic and an early diastolic murmur in a patient with definite rheumatic mitral valvular disease.

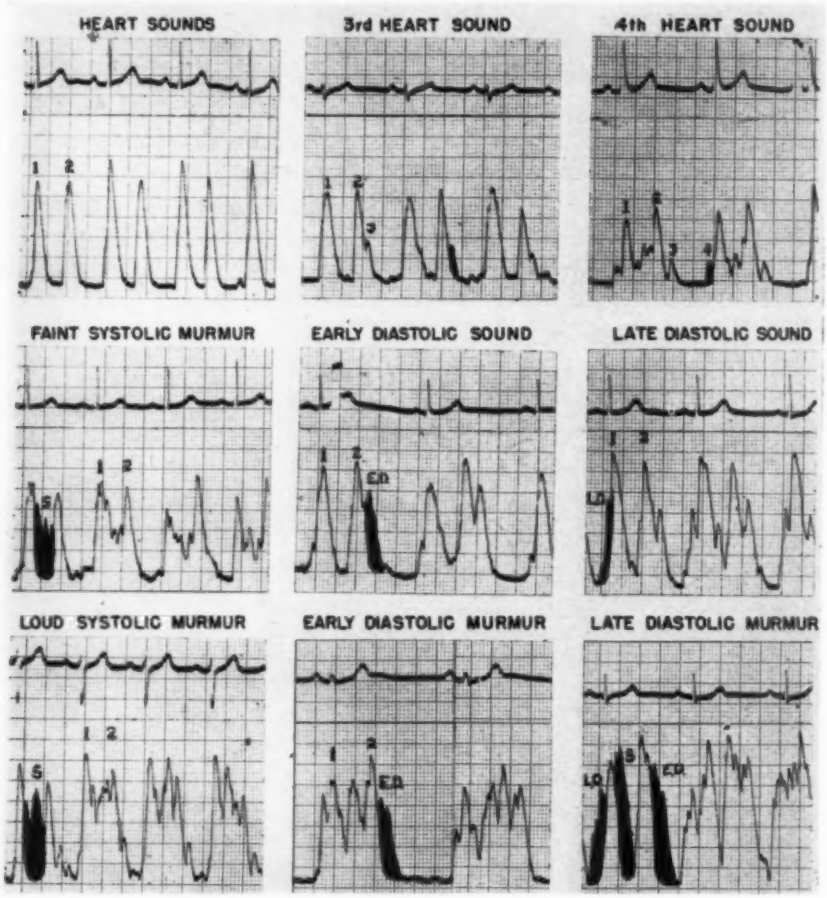

Fig. 2.—Sonvelographic records of heart sounds and murmurs. The three records on the left illustrate the first and second heart sounds, and faint and loud systolic murmurs as indicated by the black areas. The middle column illustrates early diastolic deflections produced by a third heart sound, inaudible early diastolic vibrations, and an early diastolic murmur, respectively. The three records on the right illustrate late diastolic or presystolic vibrations including auricular sounds or the fourth heart sounds and inaudible presystolic vibrations. The record in the lower right-hand corner illustrates systolic, early diastolic, and late diastolic deflections corresponding to murmurs in a patient with definite rheumatic mitral valvular heart disease.

Serial Sonvelography During Acute Myocarditis.—Serial sonvelograms during attacks of acute rheumatic fever have greater significance than individual records just as serial electrocardiograms have more value in such cases.

For example, a 7-year-old girl was carefully observed during her fifth attack of acute rheumatic fever. On admission to the hospital she had a definite systolic murmur which was loudest at the apex. The four previous attacks of rheumatic fever had left no residual diastolic murmurs which could be heard or recorded

(Fig. 3). During her stay in the hospital, she had most of the major and minor criteria of acute rheumatic fever including elevated sedimentation rate, fever, leukocytosis, polyarthritis in knees and ankles, antistreptolysin titers reaching 625 units per cubic centimeter, cardiac enlargement, and alterations in the ampli-

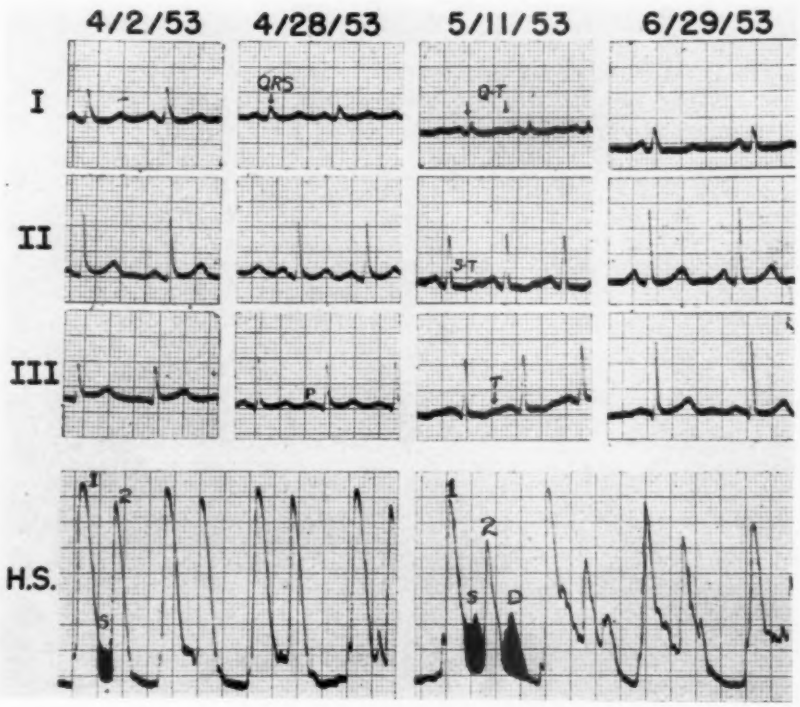

Fig. 3.—Serial electrocardiographic and sonvelographic tracings obtained in the course of a classical recurrent attack of acute rheumatic fever. The Q-T interval remained within normal limits. Note the changes in the size and configuration of P, QRS, S-T, and T. An early systolic murmur was heard and early diastolic vibrations were recorded on 5/11/53 and disappeared by 6/29/53.

tude and configuration of the P, QRS, S-T and T complexes on serial electrocardiograms (Fig. 3). Seven weeks after admission, a sonvelogram revealed an early diastolic deflection (5/11/53, Fig. 3), and an early diastolic murmur was barely audible. She was improved by June 29, 1953, and the diastolic murmur had disappeared.

This patient was selected as a clearly defined example of acute rheumatic carditis from a group of 75 patients studied during the past year. Transient early and late diastolic vibrations and murmurs have been recorded in a majority of patients during typical attacks of acute rheumatic fever even when there is every reason to believe that no chronic valvular damage has been sustained. Most of these patients display sonvelographic patterns resembling one or more of the examples used to illustrate the diastolic sounds and murmurs in Fig. 2.

Alterations in electrocardiographic and sonvelographic patterns may suggest the diagnosis of acute myocarditis when other clinical signs are equivocal as illustrated by the following case.

An 8-year-old boy was being treated for an abscessed tooth for one week prior to admission to the hospital. During this period he had leukocytosis (21,000 white blood count), elevated erythrocyte sedimentation rate (24 mm.), and fever up to 103° F. On the day before admission his right wrist and both knees were slightly tender, but this sign had disappeared by the next day and did not recur. He complained of transient pain in the chest and abdomen for

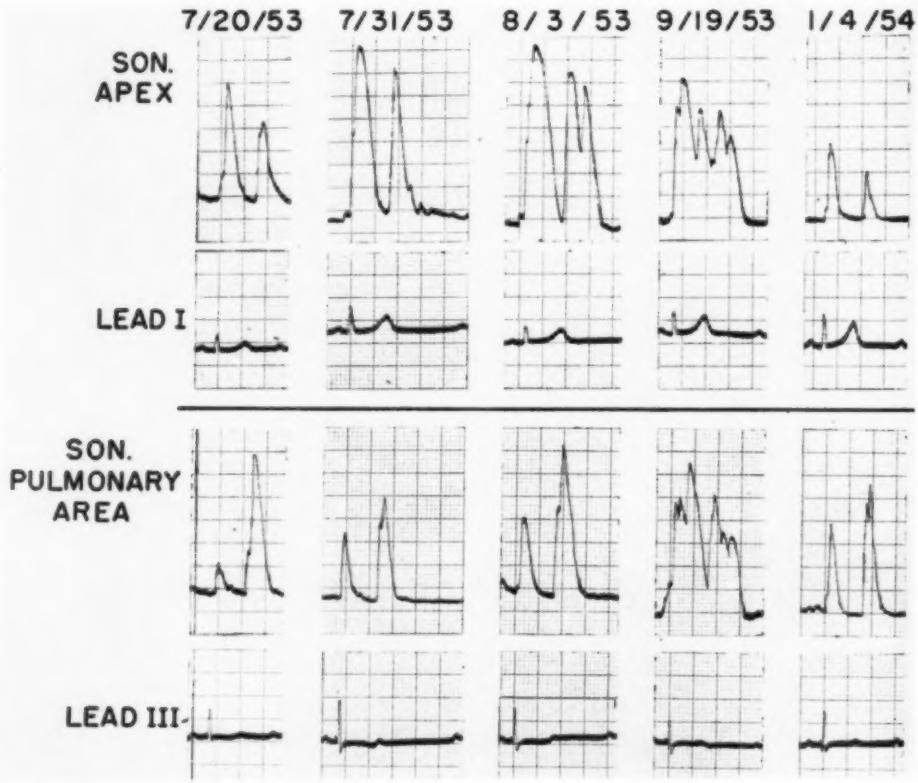

Fig. 4.—Electrocardiograms and sonvelograms from the apex and the pulmonary area were obtained on the dates indicated following a febrile illness, apparently stemming from abscessed teeth. Two months after admission (9/19/53) very prominent systolic and early diastolic deflections were recorded at a time when the patient was apparently normal. They disappeared by 1/4/54.

a few hours. The antistreptolysin titer was 166 units. The fever disappeared after five days of antibiotic therapy, and the abscessed teeth were extracted. The sedimentation rate gradually declined, and the patient became completely asymptomatic. The transient arthralgia and abdominal pain were the only clinical signs suggesting acute rheumatic fever. The fever and elevated erythrocyte sedimentation could be explained by the abscessed teeth. However, serial electrocardiograms and sonvelograms revealed changes which strongly suggested acute carditis (Fig. 4). Very definite systolic and diastolic vibrations were recorded on August 3 and September 19, 1953, disappearing before January 4, 1954. The patient was asymptomatic, and the laboratory tests were within

normal limits during the period when the sonvelograph revealed the most striking changes. Nevertheless, if these signs and symptoms had developed in a child who had previously experienced a typical attack of acute rheumatic fever, this episode would probably have been confidently labeled a recurrence of the disease. This particular episode, classified by different clinicians as no heart disease, atypical rheumatic fever, or acute nonspecific myocarditis has been selected from sixteen patients who presented serious diagnostic problems during the past year. The proper diagnosis and the optimal treatment of such cases present a most difficult problem which can only be solved by prolonged case studies in large groups of patients.

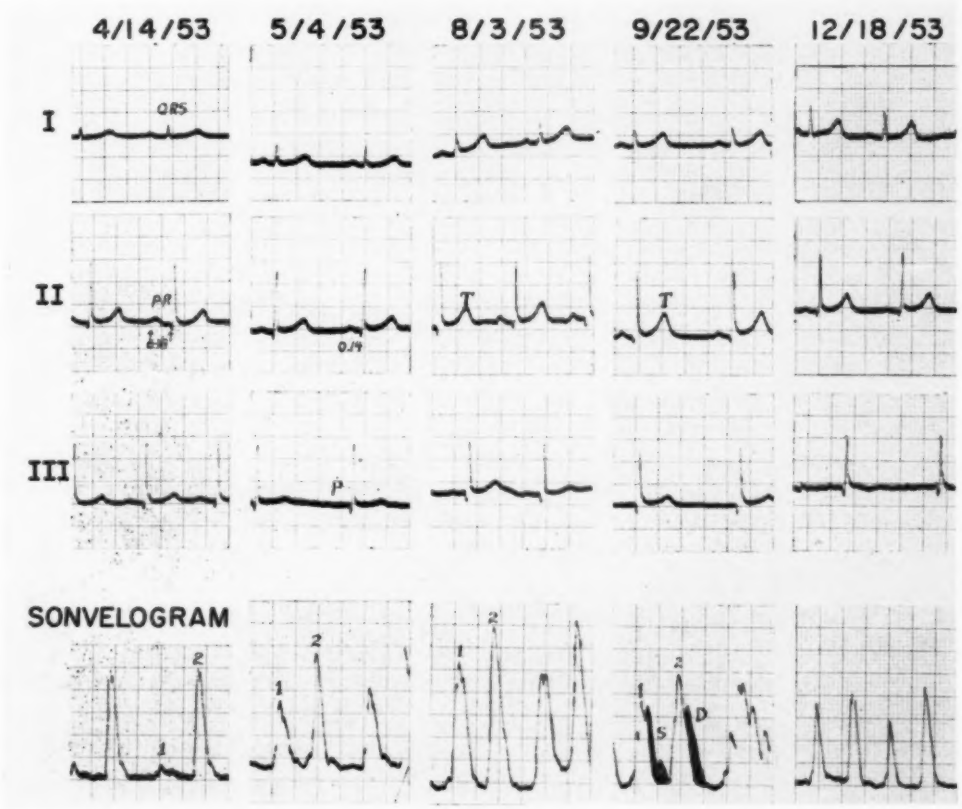

Fig. 5.—Changes in the configuration of the electrocardiographic complexes and sonvelograms occurred following a brief febrile illness characterized by mild gastrointestinal symptoms. The alterations in pattern occurred after the patient had become free of symptoms and laboratory tests were normal.

Similar changes in sonvelographic and electrocardiographic patterns have been observed in patients with no other manifestations of acute rheumatic fever. For example, a 5½-year-old girl developed a headache, vomiting, and fever (101-104°F.) of two weeks' duration. Mild diarrhea developed three days later. A wide variety of laboratory tests were normal including erythrocyte sedimen-

tation rate (14 mm.) and antistreptolysin titer (12 units). A faint short systolic murmur was noted on auscultation. The day before the fever returned to normal and the patient became asymptomatic, a muffled first sound and a faint systolic murmur were noted on the sonvelogram (4/14/53, Fig. 5). The electrocardiogram revealed a slightly prolonged P-R interval and a low potential QRS_1. During the succeeding months, the patient remained free of all symptoms and the laboratory tests remained normal, but the amplitude and configuration of P, QRS, S-T, and T complexes varied on serial electrocardiograms. Five months later the sonvelograms revealed prominent early systolic and early diastolic deflections. The systolic murmur could still be heard but the early diastolic vibrations were inaudible. The sonvelogram had cleared remarkably by December 18, 1953. This patient very likely had some form of myocarditis, either acute nonspecific myocarditis or atypical rheumatic fever. No evidence of streptococcal infection could be obtained, and the sedimentation rate was normal on repeated determinations. Furthermore, it was most disconcerting to observe objective evidence of disturbed cardiac function in a child who had no symptoms or clinical signs of disease. If neither electrocardiograms nor sonvelograms had been obtained on this patient, heart disease would have never been considered. Perhaps both the child, her parents, and the attending physician would have been better off if they had been spared inevitable doubts which have arisen. On the other hand, the possibility remains that this girl might be among the group of patients who ultimately develop valvular heart disease without a history of acute rheumatic fever.

DISCUSSION

The advent of prophylactic administration of antibiotics to prevent recurrent attacks of acute rheumatic fever has greatly increased the importance of recognizing this particular disease entity as early as possible. The diagnosis of acute rheumatic fever can be made with confidence in patients presenting a number of the major and minor manifestations of the disease.[9] Most of these criteria depend upon systemic effects of the disease which are not directly related to inflammatory lesions in the heart. According to Bland and Jones,[10] only about one-third of patients with definite attacks of acute rheumatic fever subsequently develop evidence of chronic valvular deformities, and this process apparently takes many months or years. Furthermore, clinical signs of rheumatic valvular disease disappeared over a span of 20 years in 108 out of 653 patients (16 per cent). Definite mitral stenosis has been demonstrated in the absence of heart murmurs.[11] Detection of both acute rheumatic carditis and chronic rheumatic valvular disease depends heavily upon changes in heart sounds and the development of audible murmurs. When a patient presents electrocardiographic and auscultatory signs of carditis, without associated signs of acute rheumatic fever, the condition cannot be differentiated with confidence from acute nonspecific myocarditis which may accompany a wide variety of febrile illnesses. Transient heart murmurs and alterations in electrocardiographic patterns may occur in relation to both of these conditions.

Sonvelographic records of heart sounds were routinely obtained in patients

suspected of having acute myocarditis in the hope that differences in the patterns of sound intensity would provide clues to the differentiation of acute nonspecific myocarditis from the carditis accompanying acute rheumatic fever. The simplicity of recording and interpreting sonvelographic records prompted the choice of this method instead of standard stethographic techniques for routine use. Changes in sonvelographic and electrocardiographic patterns have not demonstrated any consistent differences between patients with definite acute rheumatic fever and with "acute nonspecific myocarditis" in whom neither classical systemic signs of rheumatic fever nor streptococcal infections have been demonstrated. Three explanations may be offered for this observation: (a) the clinical differentiation between "acute nonspecific myocarditis" and acute rheumatic fever was not correct in the cases presented; (b) differences between these two conditions cannot be detected by the recording techniques employed or (c) the pathophysiologic processes in the two conditions are closely related. Only one patient in the entire series died of acute rheumatic fever and pathologic confirmation of the remaining clinical diagnoses was impossible. Since not all patients with definite attacks of acute rheumatic fever develop valvular lesions and since many of the patients with definite clinical evidence of "rheumatic" valvular heart disease have no history of acute rheumatic fever, is it not possible that the cause-and-effect relation between the two remains questionable? During the course of the present study, we were confronted by the disturbing possibility that valvular damage could conceivably result from acute nonspecific myocarditis. We have no direct evidence for or against this concept. Characteristic lesions of the valves are invariably attributed to previous acute rheumatic fever, even when there is no history of an acute attack of the disease. Are we justified in excluding the possibility that the valves develop similar damage following "nonspecific myocarditis"? The total incidence of the various disease processes which may be accompanied by signs of acute nonspecific myocarditis is so great that a very small proportion developing valvular damage from this cause could easily account for a large proportion of acquired valvular disease. It seems profitable to note that demonstrating this contingency is indefinitely precluded so long as certain characteristic inflammatory and fibrotic valvular lesions are invariably attributed to antecedent acute rheumatic fever even when the etiology cannot be established.

The authors believe that sonvelography has contributed significantly to the auscultation of heart sounds and murmurs. Having developed the technique, we are obviously biased in its favor. Recognition of the attributes and limitations of the method is of extreme importance in proper utilization. However, one observation appears clearly established, namely, when a clinician is aware that his auscultatory observations are being compared with an objective recording, the time devoted to this aspect of the physical examination increases materially. On a number of occasions, diastolic murmurs have been detected on auscultation only after the observers have been informed of the results of sonvelography. When a deflection on the sonvelograph is produced by vibrations below the threshold of audibility, clinicians may occasionally listen so intently for the sounds that they imagine they are able to hear them. This danger is inherent

in any recording device which is more sensitive than human audition. The ultimate usefulness of sonvelography must await evaluation by unbiased groups of observers.

CONCLUSIONS

1. Direct recording of the envelope of heart-sound intensity (sonvelography) provides simple patterns which indicate changes in the intensity of heart sounds and the presence of heart murmurs. Used as a guide to auscultation, this method may facilitate detection of low-frequency murmurs which are just above the level of audibility. The technique is sufficiently simple to be applied simultaneously with routine electrocardiography. The advantages and limitations of sonvelography were discussed.

2. Most patients with acute myocarditis develop a deflection in early diastole representing vibrations which may or may not be audible. In some cases, these deflections represent third heart sounds; in others, early diastolic murmurs are audible. Typical patterns observed in cases with clinical signs of acute rheumatic fever were presented along with a more detailed consideration of a specific case.

3. Alterations in the electrocardiographic and sonvelographic patterns simulating those accompanying acute rheumatic fever may occur in patients without clear-cut clinical signs of acute rheumatic fever. Such patients may be regarded as suffering from acute nonspecific myocarditis or atypical rheumatic fever. Two such patients were discussed and the problems involved in arriving at a specific diagnosis were emphasized.

This study was accomplished only through generous cooperation by the staff of the Children's Orthopedic Hospital, and Mrs. Miriam Grapp, who recorded all the tracings presented in the report.

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STUDIES WITH THE DISPLACEMENT, VELOCITY, AND ACCELERATION BALLISTOCARDIOGRAPH IN AORTIC INSUFFICIENCY

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THE clinical picture of aortic insufficiency usually presents no great difficulty in diagnosis. The signs and symptoms have been described many times in the literature. The presence of a high-pitched aortic diastolic murmur, a large pulse pressure, and a low diastolic pressure with capillary pulses is classical and rarely missed by the clinician. There are many cases of mild aortic incompetence, however, which present some difficulty to recognize. The ballistocardiograph findings in our laboratory in aortic insufficiency seem to be quite specific and of great diagnostic value, especially on the acceleration curves. The acceleration ballistocardiograph would appear to provide a sensitive measure for demonstrating small aortic valvular leaks and thus may be of value to the clinician in the difficult cases.

METHODS AND MATERIALS

The instrument and techniques used in this study have been previously described in detail.[1,2] The simultaneous recording of displacement, velocity, and acceleration was obtained by using calibrated instruments. The platform on the legs holding the magnet was kept at a frequency of about 30 cycles. By use of this technique, a close approximation of the measurement of body motion as a single degree of freedom can be maintained up to approximately 10 cycles in most instances. The studies were done after a rest period of 10 minutes and at least three hours following a meal. Ten cases of aortic insufficiency were studied, varying from extremely mild cases to severe, but all cases were compensated at the time of examination.

In a previous paper,[3] publication of the ballistic traces of fifty normal adults between 30 and 40 years of age were used for normal standards. However, the weight of the platform was three pounds and the natural frequency of the calibrated instruments on the legs was kept between 16 and 20 cycles by using a segment of elastic stocking between the platform and the skin of the legs. An analysis of the platform frequency[2] showed that this may be too close to the

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natural frequency of the body in some cases. The same type of calibrated instrumentation has been redesigned, using a lighter magnet and platform (10 ounces) so that the frequency of the platform could be maintained at about 30 cycles per second. The normal standards presented in this paper were made with the 10-ounce platform. Also, studies have shown in our laboratory that the amplitudes of the ballistic tracings for patients between 20 and 30 years of age are similar to those of the 30 to 40 age group, so the sample of fifty normal people used in this study is from normal adults between the ages of 20 to 40 years.

The instrumentation is calibrated so that the displacement trace = 0.0002 inch per chart mm. (0.005 mm.). The velocity trace = 0.1 mm./sec. per chart millimeter and the acceleration trace = 3.0 mm./sec.^{2} per chart millimeter. All values of amplitudes are expressed as absolute values based on this calibration and a natural frequency of the platform between 25 and 30 cycles, as mounted on a segment of elastic stocking between the platform and skin over the legs. The feet, with the shoes on, were suspended from a footrest with flexible side supports. (A flexible side support allows the foot to seek its own level of comfort and thus reduces body ambient vibration interference.) Contact was between the heel of the shoe and the footrest, and the calves were not permitted to touch the table. These standards are based on measurements taken with respiration suspended during expiration.

The normal standards in this paper are based on sound analytical principles from the viewpoint of vibration measurement. This means that any clinician using the Dock type leg-mounted pickup, who will use the same footrest and calibrated type of instrumentation and maintain a high natural frequency in the platform between 25 and 30 cycles, should be able to utilize these standards and obtain reasonable reproduction of these results. This should be a significant advance in method for ballistocardiography.

It should be pointed out, however, that variation in the body-damping coefficients can also produce variation in amplitudes for the same applied internal forces. Our studies of body damping, however, have shown that the ratio of actual to critical damping is quite similar from person to person in the age groups of 20 to 40 and significantly higher damping coefficients seem to occur for practical purposes over 45 years of age. In the age groups tested, some variation in amplitudes could be expected from damping differences, but this does not seem to be of great significance. The damping tests showed only slight variations; all values of damping for the group were between 0.3 and 0.4 of critical. Since the linearity of the body spring system has not been proved, all tests presently used for estimating damping must be viewed with some caution and restraint. The tests for body damping were done on the velocity curves by attenuating the signal twenty-five times (x4 to x100) and displacing the body and releasing it suddenly (Head Push Test). By measuring the oscillatory decay pattern, damping values were established.

The fifty normal subjects used in this study were, in general, different people from those used in a previous paper.[3] However, several of our higher amplitude normal individuals were repeated and included in this study to show the influence of low platform frequencies on amplitude.

One subject, who showed the highest amplitude of the initial group of fifty, had an IJ displacement (peak of I wave to peak of J wave) of 0.0036 inch. This subject showed a body displacement of 0.0028 inch when repeated in this study with the newly designed instrument and a natural frequency of the platform above 25 cycles. Previously, with the magnet and suspension weighing three pounds on an elastic stocking, the platform frequency was 14 cycles in this case, which illustrates that the low platform frequency contributed appreciably to the amplitude and proves that a lower platform frequency (below 25 cycles) would be misleading for recording body motion from some individuals due to a loose spring coupling on the shins. However, in general, the amplitudes of this group showed close agreement when compared with the previous group of normal individuals.

NORMAL BALLISTOCARDIOGRAPH STANDARDS FOR 50 NORMAL ADULTS BETWEEN 20 AND 40 YEARS OF AGE

Age: Mean—33.48; Standard Deviation—3.9
Weight: Mean—157.46 pounds; Standard Deviation—20.5 pounds
Height: Mean—68.88 inches; Standard Deviation—2.33 inches
Body Frequency: Mean—4.3 cycles; Standard Deviation—0.37 cycles

Displacement:

Amplitude: IJ Segment = Mean Value = 0.00214 inch
Standard Deviation = 0.0003 inch

Wave Ratio Measurements

Mean	Standard Deviation
Percentage HI of IJ	
51	4.7
Percentage JK of IJ	
105	7.4

Timing

	Mean	Standard Deviation
R-K	0.36	0.019
R-J	0.25	0.015
R-I	0.17	0.01
R-H	0.10	0.01
HI segment	0.066	0.008
IJ segment	0.087	0.008
JK segment	0.100	0.01

Velocity:

Amplitude: IJ Segment = Mean Value = 1.4 mm./sec.
Standard Deviation 0.22= mm./sec.

JK Segment = Mean Value = 1.69 mm./sec.
Standard Deviation=0.29 mm./sec.

Wave Ratio Measurements

Mean	Standard Deviation
Percentage HI of IJ	
54	6
Percentage JK of IJ	
121	8

Timing

	Mean	Standard Deviation
R-K	0.301	0.016
R-J	0.209	0.012
R-I	0.138	0.009
R-H	0.075	0.010

Maximum Inspiration
JK. Mean=1.83 mm./sec.
Standard Deviation=0.42 mm./sec.

Minimum Expiratory
JK. Mean=1.16 mm./sec.
Standard Deviation=0.29 mm./sec.

Acceleration:

IJ segment = Mean = 57 mm./sec.^{2} (19 mm.)
= Standard Deviation = 10.5 mm./sec.^{2} (3.5 mm.)

JK segment = Mean = 68.4 mm./sec.^{2} (22.8 mm.)
Standard Deviation = 11.0 mm./sec.^{2} (3.7 mm.)

KL segment = Mean = 54.9 mm./sec.^{2} (18.3 mm.)
Standard Deviation = 10.5 mm./sec.^{2} (3.5 mm.)

R to H peak = Mean = 0.047
Standard Deviation = 0.015

Ratio of J to K peak (from base line) = Mean = 0.84
Standard Deviation = 0.13

Amplitude from base line:

H peak = Mean = 9.3 mm./sec.^{2} (3.1 mm.)
= Standard Deviation = 2.6 mm./sec.^{2} (.88 mm.)

I peak = Mean = 19.2 mm./sec.^{2} (6.4 mm.)
= Standard Deviation = 5.4 mm./sec.^{2} (1.8 mm.)

J peak = Mean = 36.9 mm./sec.^{2} (12.3 mm.)
= Standard Deviation = 6.9 mm./sec.^{2} (2.3 mm.)

K peak = Mean = 30.9 mm./sec.^{2} (10.3 mm.)
= Standard Deviation = 6.0 mm./sec.^{2} (2.0 mm.)

L peak = Mean = 25.2 mm./sec.^{2} (8.4 mm.)
= Standard Deviation = 5.4 mm./sec.^{2} (1.8 mm.)

Timing: Peak of I to J peak
Mean = 0.060 sec.
Standard Deviation = 0.009 sec.

Peak of J to K peak
Mean = 0.081 sec.
Standard Deviation = 0.008 sec.

Maximum inspiratory—JK
Mean = 77.7 mm./sec.^{2} (25.9 mm.)
Standard Deviation = 13.5 mm./sec.^{2} (4.5 mm.)

Minimum expiratory—JK
Mean = 49.2 mm./sec.^{2} (16.4 mm.)
Standard Deviation = 9.9 mm./sec.^{2} (3.3 mm.)

Maximum inspiratory—BK (Base line to K peak)
Mean = 35.1 mm./sec.^{2} (11.7 mm.)
Standard Deviation = 6.6 mm./sec.^{2} (2.2 mm.)

Minimum expiratory—BK
Mean = 21.3 mm./sec.^{2} (7.1 mm.)
Standard Deviation = 5.4 mm./sec.^{2} (1.8 mm.)

The standards for these normal subjects were based on simultaneous recording of displacement, velocity, and acceleration. These standards could also be used for single-channel type recordings.

When complex hemodynamic alterations are studied, the acceleration curves are extremely sensitive and valuable. The interpretation of acceleration measurements, however, may be impossible without a simultaneous displacement curve. For full clinical interpretation, it will be necessary to record a displacement curve simultaneously with the acceleration curves, as many cases (such as mitral stenosis) show a high-amplitude chaotic type of wave which is nearly impossible to understand unless a simultaneous displacement trace is available for reference.

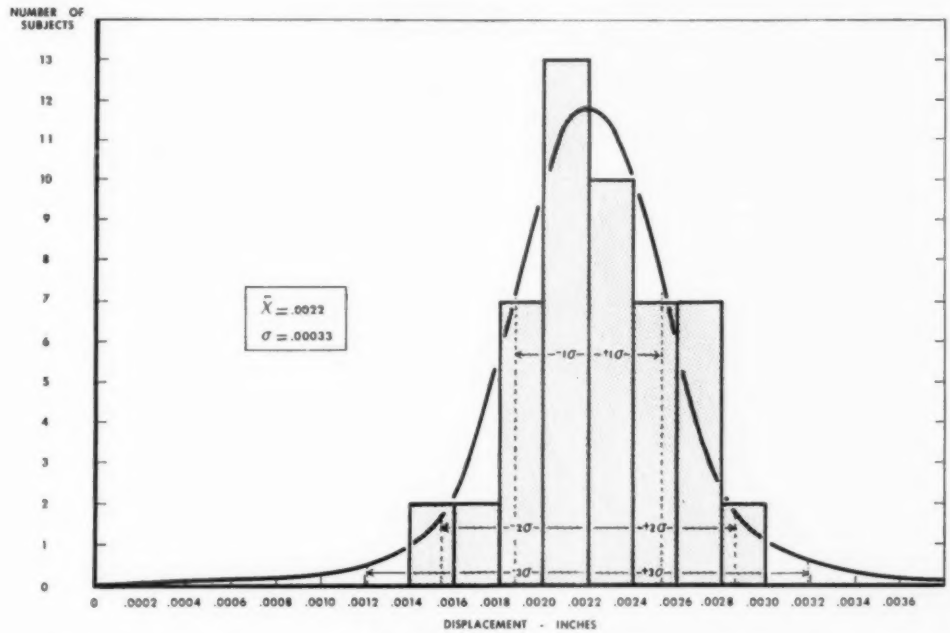

Fig. 1.—Frequency distribution curve of body displacement reflected in ballistocardiographic tracings, indicating range of standard deviations, for fifty normal subjects between the ages of twenty and forty.

The plot of the displacement IJ amplitudes is illustrated in Fig. 1. The three highest and three lowest amplitudes in the normal group of the displacement IJ segment are illustrated in Fig. 2.

DISCUSSION OF RESULTS

A sample of fifty normal people between the ages of 20 and 40 was chosen to determine the normal standards for body displacement. The selection of body displacement as an index for measurement was made in view of the fact that this aspect of ballistocardiography is the most universally known.

The accompanying graph shows that the range of displacement is from 0.0014 inch to 0.0028 inch, with a mean of 0.0022 inch and a standard deviation

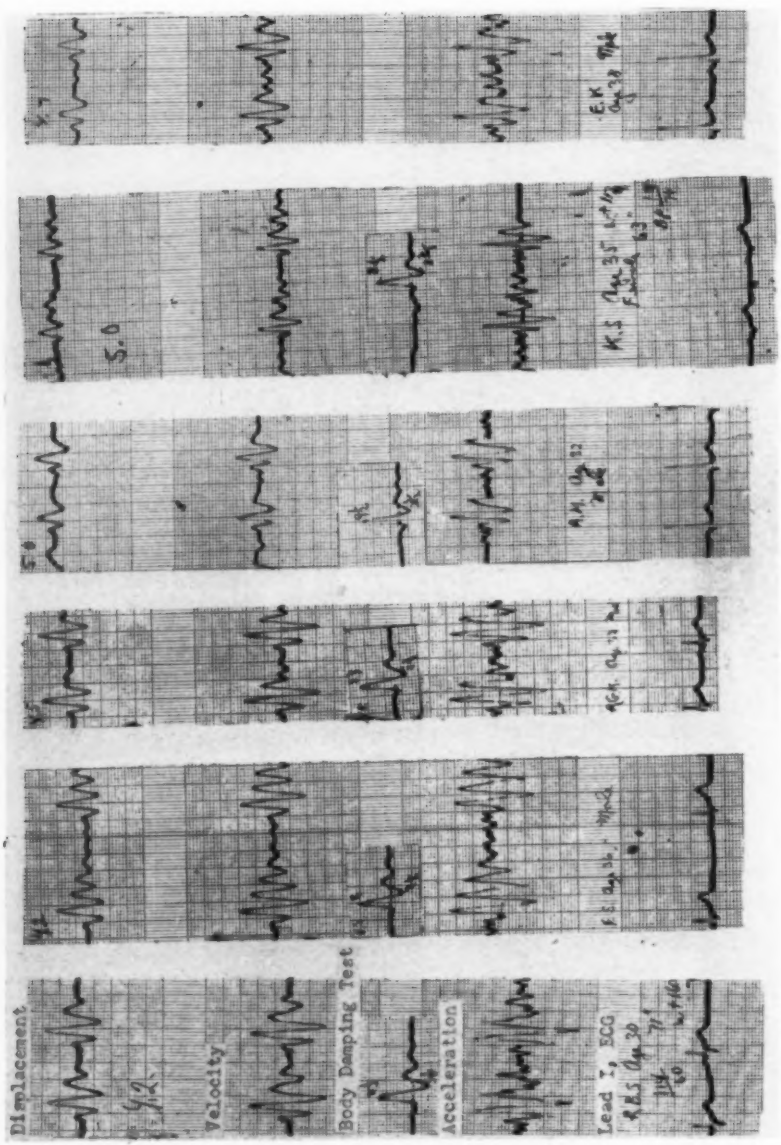

Fig. 2.—Illustration of the displacement, velocity, and acceleration curves of the three highest and three lowest amplitudes of IJ displacement in fifty normal subjects. The body damping tests are inserted between the velocity and acceleration curves. The three highest amplitudes are in the first column on the left side of the photograph. The displacement, velocity, and acceleration curves are illustrated from above downward, so that the displacement curve is at the top of the figure.

of 0.00033 inch. The curve best describing the data was found to be a normal type distribution curve.

This sample of fifty normal subjects can be considered a fairly good representation of the total population for the age groups that have been studied. It is realized that amplitudes decrease with advancing age, and thus much further study will be necessary for establishing standards for the older age groups. The sample standard deviation equals 0.00036, while the estimated population standard deviation equals 0.00035.

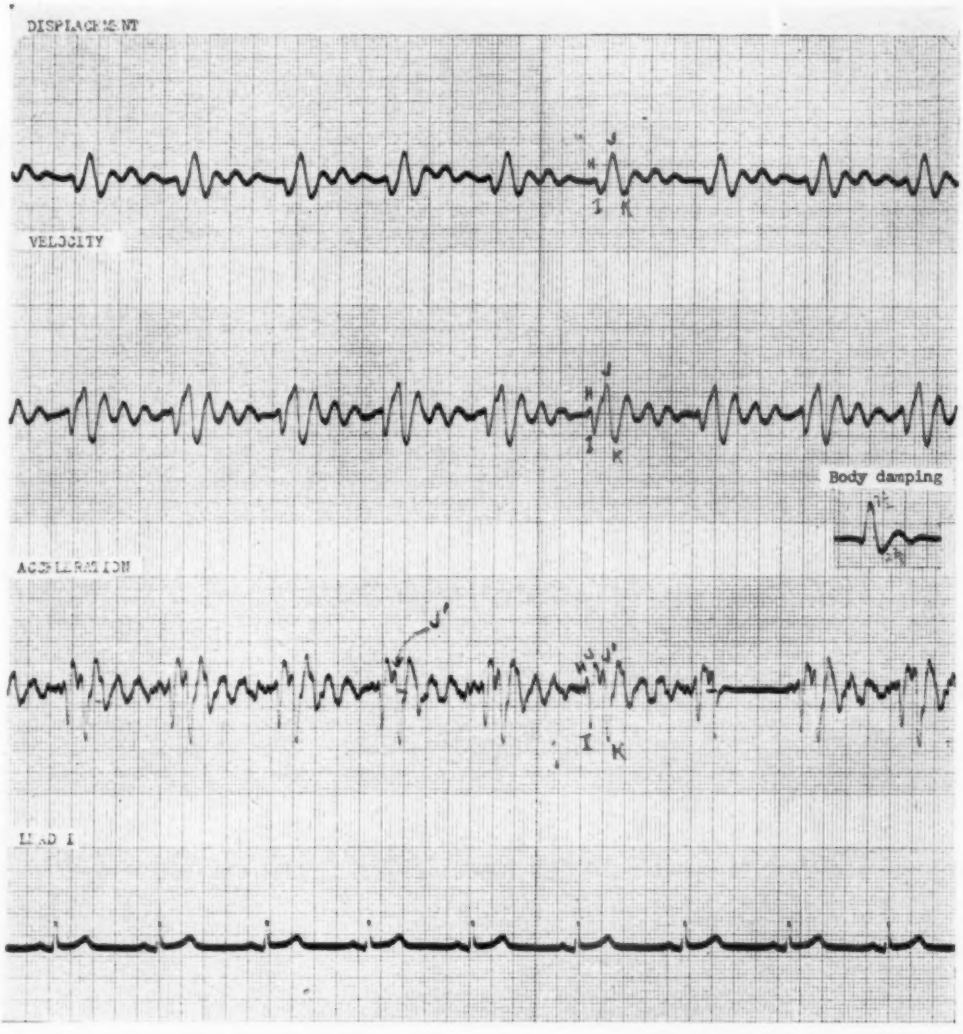

Fig. 3.—A 28-year-old male with aortic insufficiency, blood pressure 136/44 mm. Hg. Note J′ notch on the acceleration curve. There was no clinical evidence of incapacity in this case.

The computed standard error of the mean $\sigma_{\bar{x}} = 0.00005$) indicates that the true population from which this sample has been selected will not vary from the

range of 0.00199 to 0.00229 in 99 per cent of the cases; hence, this sample of fifty is adequate.*

A sample of ten subjects with aortic insufficiency showed a mean displacement of 0.00338 (far in excess of the 0.00214 inch for the normal group). No further statistical comparison could be made, however, due to the smallness of the size of the aortic insufficiency group.

ANALYSIS OF TEN CASES OF AORTIC INSUFFICIENCY

Mean Age, 33

Displacement: IJ = Mean Value = 0.0034 inch
Highest 0.0056 inch (1 case); lowest 0.0020 inch (1 case)
Ratio of HI to IJ segment = Mean Value = 33 per cent
Highest 44 per cent (1 case); lowest 25 per cent (1 case)
Ratio of JK to IJ segment = Mean Value = 119 per cent
Highest 133 per cent (1 case); lowest 105 per cent (2 cases)

Timing

	Mean
Peak of R to K peak	0.34 second
R to J peak	0.23 second
R to I peak	0.14 second
R to H peak	0.05 second

Since the number of cases is too small for standard deviation or accurate statistical analysis, it should be mentioned that, in general, the more severe clinical cases had more rapid timing to all peaks. Thus, in five cases the RK was between 0.31 and 0.33 second.

Velocity:

IJ segment = Mean Value = 2.0 mm./sec.
Highest 3.5 mm./sec. (1 case); lowest 1.2 mm./sec. (1 case)
JK segment = Mean Value = 2.98 mm./sec.
Highest, over 5.0 mm./sec. (1 case); lowest 1.4 mm./sec. (1 case)
Ratio of HI to IJ segment = Mean Value = 37 per cent
Highest 52 per cent (1 case); lowest 26 per cent (1 case)
Ratio of JK to IJ segment = Mean Value = 154.0 per cent
Highest 188 per cent (1 case); lowest 117 per cent (1 case)

Timing

	Mean
RK	0.28 second
RJ	0.20 second
RI	0.11 second
RH	0.04 second

Acceleration:

JK (peak of J to peak of K) = Mean Value = 107 mm./sec.^{2}
Highest, over 150 mm./sec.^{2} (1 case); lowest 60 mm./sec.^{2} (1 case)
Base line to K peak = Mean Value = 66 mm./sec.^{2}
Highest, over 90 mm./sec.^{2} (3 cases); lowest 33 mm./sec.^{2}
Ratio of acceleration J peak to K peak (above and below the acceleration base line) = Mean Value = 1.65 per cent
Highest 1.9 per cent (2 cases); lowest 1.3 per cent (1 case)

*It has been necessary to carry these calibrations to five decimal places through standard statistical procedures; however, it is realized that this degree of accuracy cannot be ascertained in practical clinical application.

CASE REPORTS

CASE 1.—J. S., aged 28, male, blood pressure 136/48 mm. Hg. This case has no history of rheumatic fever and has had no complaints referable to the cardiovascular system. Served four years in the Pacific in World War II. On routine examination for service, a Grade 2 systolic and diastolic murmur heard best at the aortic area was found. A diagnosis of mild aortic insufficiency had been made. This case had normal electrocardiogram and exercise test and no limitation of

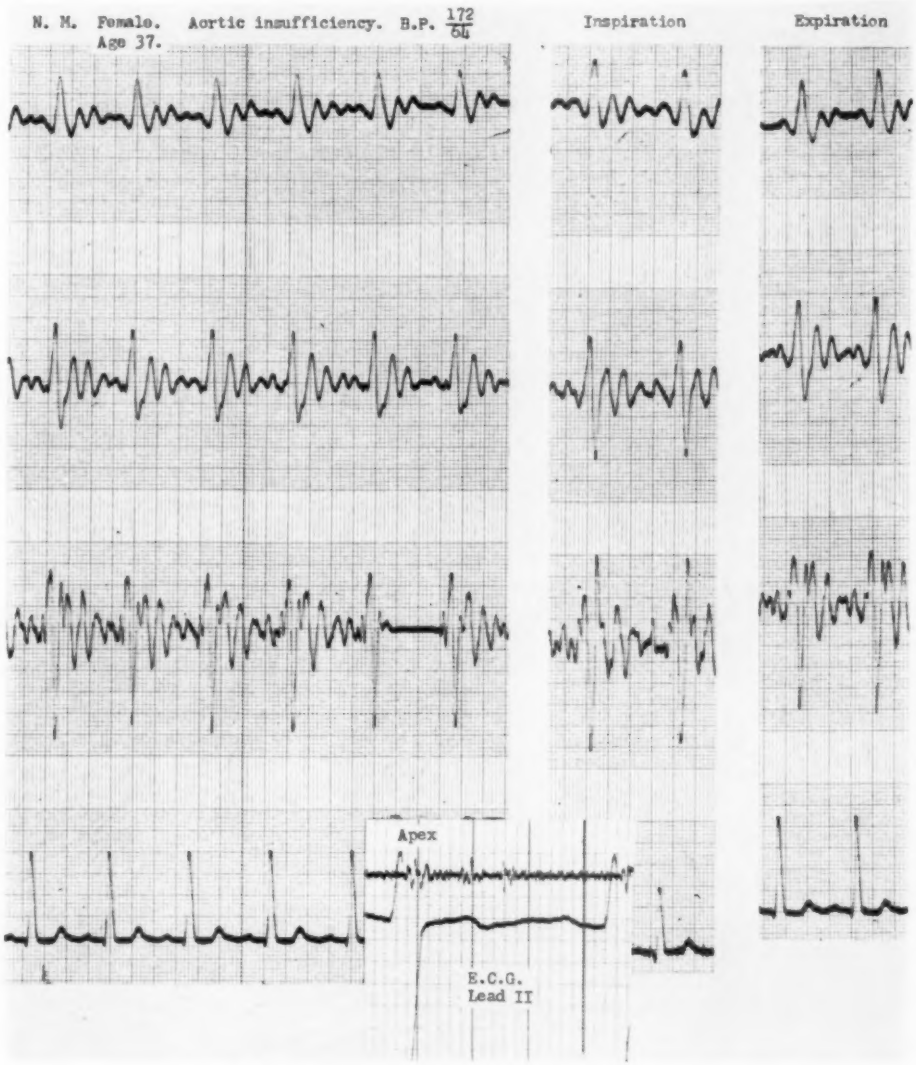

Fig. 4.—A 37-year-old female with aortic insufficiency. Note the normal amplitude in the displacement curve but rapid timing to wave peaks. Note also that acceleration base line to K peaks is extremely high amplitude and exceeds the third standard deviation from normal.

activity. From the clinical point of view, it was felt that this man had the least disturbance of function in the ten cases studied. The ballistic amplitudes are normal, but the notched J′ wave is seen as well as an increased J to K ratio, 1.6 in this case. The ballistocardiograph is illustrated in Fig. 3.

CASE 2.—N. M., aged 37, female, blood pressure 172/64 mm. Hg. This patient had rheumatic fever at the age of 10. Since that time she has known that a valvular disorder has been present and complains only of dyspnea on exertion. Functionally, this patient has been able to work and has only functional limitation on moderate exertion. Systolic and diastolic murmurs Grade 2, heard best at the aortic area. Electrocardiogram showed evidence of left ventricular hypertrophy and mild strain with QRS of 0.12 second. The ballistocardiograph is illustrated in Fig. 4. The displacement IJ was within normal limits; however, the notching is present on the upstroke of the acceleration J wave, and the acceleration base line to K peak is of high amplitude, 66 mm./sec.^{2} with a ratio of J to K of 1.7 per cent.

These two cases show the lowest amplitudes of displacement IJ of the group of aortic insufficiencies and were within normal limits. It can readily be seen that if the displacement curves only were recorded, very little, if any, clinical data would be apparent in these cases.

CASE 3.—B. C., aged 34, Negro, blood pressure 170/60 mm. Hg. This patient had rheumatic fever in childhood. Systolic and diastolic murmurs, heard best at the aortic area, were present. This case was complicated by the presence of sickle cell anemia, hemoglobin, 8 grams; red blood count, 2,300,000.

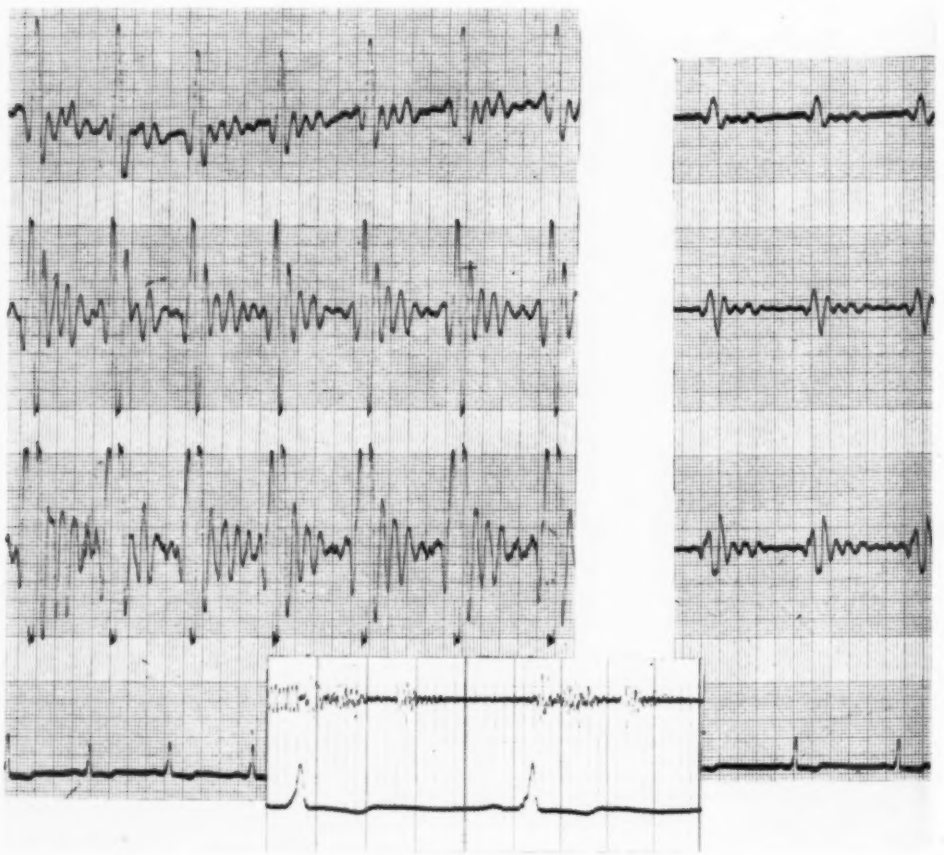

Fig. 5.—A 34-year-old male with blood pressure 170/60 mm. Hg. with aortic insufficiency and sickle cell anemia. This case had the most functional disturbance of ten series of cases. Note the notching on the acceleration J wave when the platform frequency is lowered and the signal attenuated five times. This is illustrated on the right-hand side.

This case showed the highest amplitudes of the aortic insufficiency cases. Moderately severe incapacity was present, and exercise tolerance was limited. Electrocardiogram showed evidence of left ventricular strain pattern. The J prime notch could not be seen on the tracing with a high

natural frequency of the platform. By attenuating the signals five times and using a lower platform frequency by adding weight to the platform on the legs (approximately 20 cycles), the notching can be seen on the upstroke of the acceleration J wave. The base line to K peak measurement on the acceleration curves was over 90 mm./sec.^{2} The ratio of acceleration J to K peak was 1.6. This case is illustrated in Fig. 5.

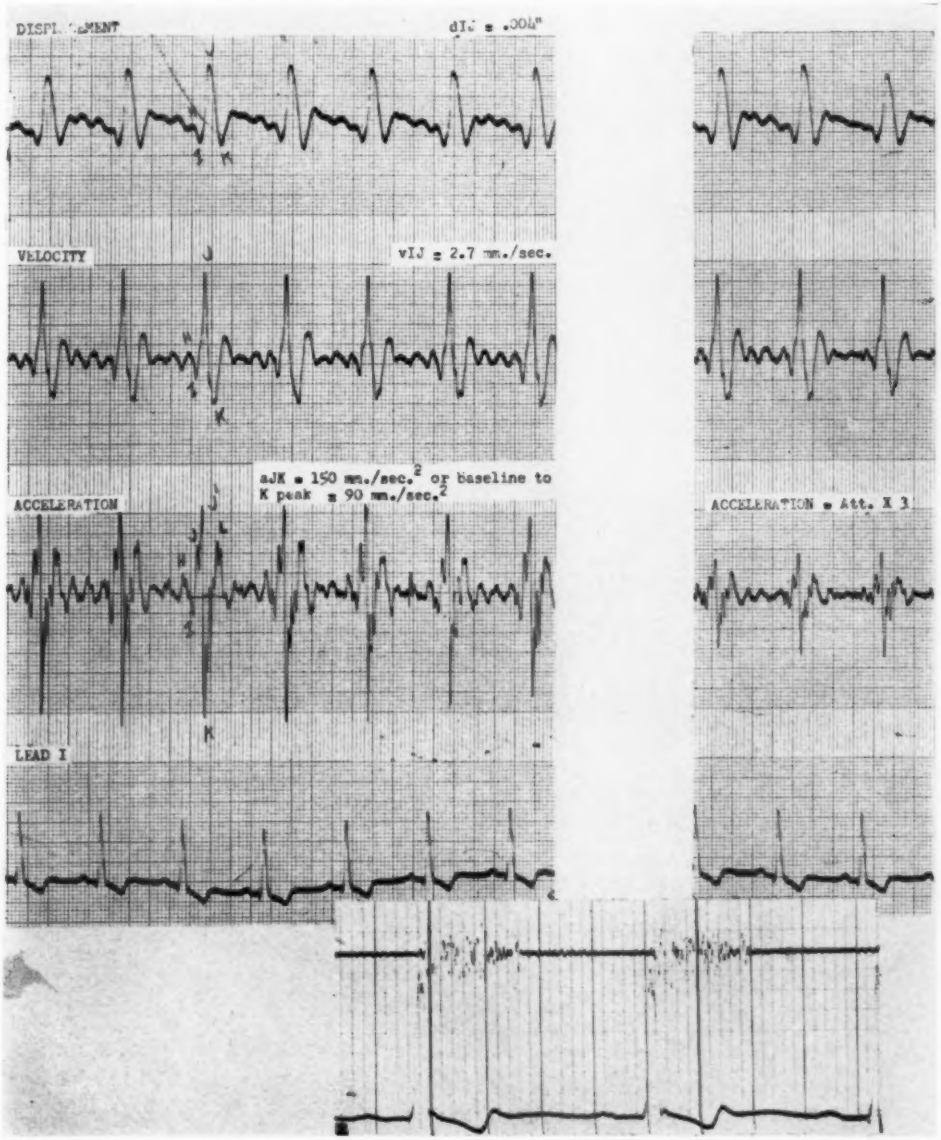

Fig. 6.—A 37-year-old male with aortic insufficiency and probable mitral regurgitation. Note the high amplitude J′ notch on the acceleration curves.

CASE 4.—R. W., aged 37, male, blood pressure, 140/62 mm. Hg. This patient had rheumatic fever in childhood. The systolic murmur was heard best at the apex, and a low grade diastolic murmur was heard best at the third left intercostal space. The possibility of a combined mitral and aortic lesion could not be excluded in this case. This patient is working regularly but has moderately severe dyspnea on moderate exertion. He has no complaints other than limitation of

activity. The electrocardiogram showed patterns typical of left ventricular strain and hypertrophy. The displacement curves show high amplitudes IJ segments, 0.004 inch with low HI of IJ ratios. The velocity curve shows high amplitude IJ and JK segments. The acceleration curves show high amplitudes with base line to K peak of 90 mm./sec.^{2} The J′ notch is very prominent and associated with a J to K ratio of 1.4. This case is illustrated in Fig. 6.

CASE 5.—J. A. F., aged 24, male, blood pressure, 120/62 mm. Hg. This patient was an applicant for pilot certification. No history of rheumatic or syphilitic disease. However, an extremely high-pitched diastolic murmur could be heard at the aortic area only on standing. A funnel chest deformity was present with evidence of fusiform dilatation of the aorta on x-ray and some evidence of the facies of arachnodactyly (Marfan's syndrome). The electrocardiogram was normal and limitation of activity was only mild, although fatigue was a prominent symptom.

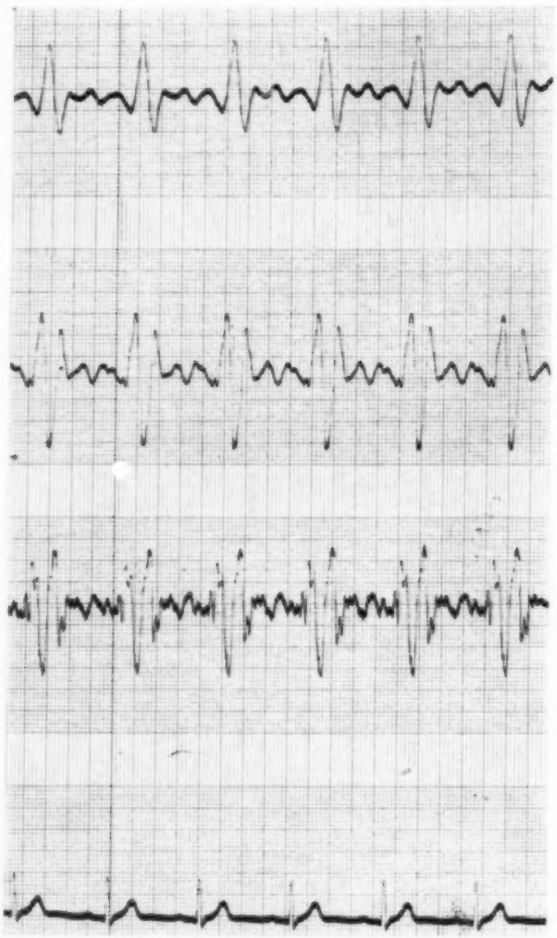

Fig. 7.—J.F. A 24-year-old male with aortic insufficiency and blood pressure 120/62 mm. Hg. Possibly Marfan's syndrome. Note the J′ notch on the acceleration curves and deep velocity K wave.

This case shows high amplitude displacement IJ segment with deep JK segment. The velocity curve shows a deep JK segment and JK of IJ ratio was 188 per cent. Note the peculiar destruction and notching of the H wave. The acceleration curves show deep base line to K peak measurement, 48 mm./sec.^{2} and a notched J′ wave. The ratio of J to K peak was 1.4 per cent. This case is illustrated in Fig. 7.

The diagnosis of this case had been previously missed on two different examinations. In this type of case, where signs and symptoms are not clear-cut, the ballistocardiogram may prove to be extremely valuable.

When the above cases are compared to the normal standards group, several important differences become obvious. In general, nearly all cases of aortic insufficiency had higher amplitudes in all measurements than the normal group.

Displacement comparisons were not diagnostic in these cases, but some deviations from normal were present, thus: (1) The ratio of HI to IJ segments was low when compared to that of normal subjects with a mean of 33 per cent compared to 51 per cent, but there was some overlap between normal and abnormal in the milder cases. (2) The ratio of JK to the IJ segment was higher in aortic insufficiency, mean of 119 per cent compared to 105 per cent, but overlap between normal and abnormal was present. (3) The timing from the R peak to the HIJK displacement peaks was more rapid in aortic insufficiency than in normal individuals, and in general the more severe the leak, the more rapid the timing.

Velocity comparisons were, in general, similar to displacement records. However, the ratio of velocity JK to IJ showed changes that may be of clinical value.

The mean JK of IJ ratio in normal individuals was 121 per cent, and the mean in aortic insufficiency was 154 per cent. All but two cases of aortic insufficiency exceeded 137 per cent (standard deviation was 8 per cent in normal subjects) and seven cases exceeded 145 per cent, so that all but three cases of aortic insufficiency exceeded the third standard deviation of the normal group. This would seem to have clinical value and probably represents the increase in the velocity head that takes place in the aorta and femoral arteries in aortic regurgitation.

Acceleration comparisons seem to be more valuable from the clinical point of view. The acceleration K peaks when measured from the base line seem to be extremely sensitive to the dynamic alterations in aortic insufficiency. The mean value of base line to K peak in normal individuals was 30.9 mm./sec.^{2} The mean value of ten cases of aortic insufficiency was 66.3 mm./sec.^{2}

All but one case ot aortic insufficiency exceeded 42 mm./sec.^{2} (standard deviation in normal individuals was 6.0 mm./sec.^{2}) and there seemed to be strong relationship between the measurement and clinical evaluation. In other words, the higher the amplitude, the more severe were clinical symptoms.

If the acceleration J and K peaks were measured from the base line and a ratio of one amplitude to the other was established, it was possible to completely separate the normal from the abnormal group. In the normal group, the mean value of accleration J to K peak ratios was 0.84 with a standard deviation of 0.13. The mean value of this measurement in ten cases of aortic insufficiency was 1.65 with a low of 1.3 in one case and a high of 1.9.

In coronary disease, the ratio of the acceleration J to K peak is usually low and under 0.50. This would seem to emphasize the value of this measurement, since the hemodynamics are opposite (the coronary has low forces of ejection, and the aortic insufficiency has high forces of ejection).

HARMONIC ANALYSIS

In our studies of the acceleration pattern obtained from cases of aortic insufficiency, definitive notch patterns have been noted which indicated the possibility of significant contributions from high-frequency components of the motion. In order to determine whether this notching was in fact due to the high-frequency components or whether it was due to the magnitude and phase lag of specific components in the acceleration ballistic complex, a Fourier wave analysis was performed for two cases of aortic insufficiency and one case of healed anterior infarct. Table I gives the order, frequency in cycles per second, and amplitude of each component for the three cases investigated.

TABLE I

COMPONENT	CASE 1 AORTIC INSUFF.		CASE 2 AORTIC INSUFF.		CASE 3 HEALED ANT. INFARCT	
	FREQUENCY (C.P.S.)	AMPLITUDE	FREQUENCY (C.P.S.)	AMPLITUDE	FREQUENCY (C.P.S.)	AMPLITUDE
1	1.32	0	1.19	10	1.10	10
2	2.64	0	2.38	0	2.20	10
3	3.96	40	3.57	30	3.30	25
4	5.28	100	4.76	75	4.40	30
5	6.60	90	5.95	100	5.50	60
6	7.92	90	7.14	65	6.60	100
7	9.24	0	8.33	50	7.70	100
8	10.56	0	9.52	20	8.80	80
9	11.88	0	10.71	0	9.90	0

It is recognized that the sampling involved herein is too small to warrant drawing any conclusions. However, it may be noted that for the cases examined, the notch pattern does not appear to be associated with high-frequency components since nothing above 10 c.p.s. appears significant. Nickerson and Mathers[4] in a similar harmonic analysis of seven cases (6 normal subjects and 1 coarctation of the aorta) found significant frequency components, in the acceleration records, up to 11 c.p.s. Thus, the significant components in our three cases are of the same order as that found for the normal individuals, and it can therefore tentatively be concluded that the unique notch pattern for the cases of aortic insufficiency are associated with phase lag and magnitude of specific low-frequency components of the acceleration.

It may be noted that Nickerson[5] has published similar tracings in aortic insufficiency. The most striking features of his records were their unusual size when compared with those of normal people and the appearance in many records of a slurring on the rising limb of the J wave.

DISCUSSION

One of the major difficulties encountered in ballistocardiography stems from the fact that the significant frequency components in the cardiovascular force

are approximately equally distributed below and above the natural frequency of the body. This results in a nonlinear response of the displacement of the body, with amplification of the frequency components below the body natural frequency, and attenuation of the high-frequency components. It is possible to overcome to some extent the attenuation of the high-frequency components by the proper choice of platform frequency, since a low platform frequency yields a rising response which in turn tends to compensate for the body attenuation. Although the frequency parameter δ (ratio of platform frequency to body frequency) should not be lower than 6 for consistent quantitative measurements of the

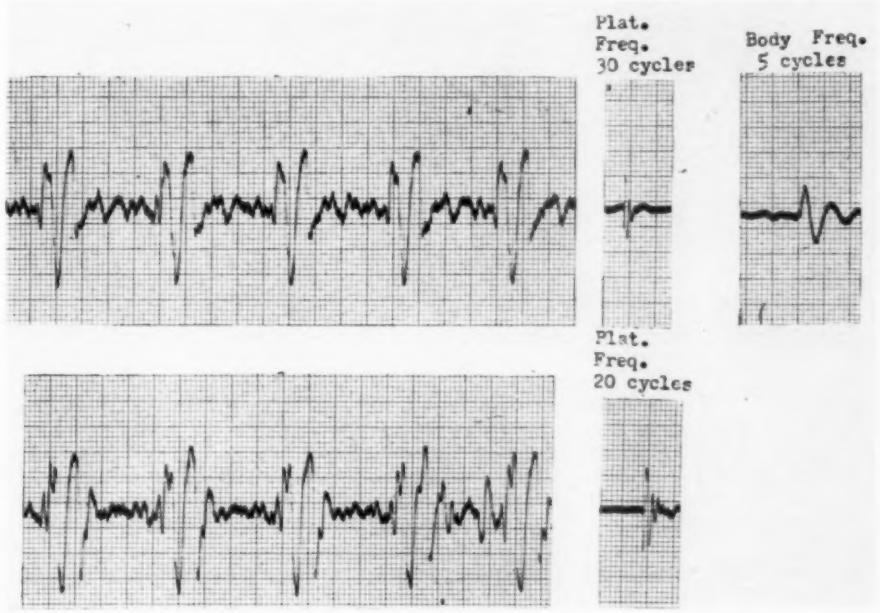

Fig. 8.—J.F. This is the same case as illustrated in Fig. 7, taken two months later. Note that the notching of the acceleration J peak is amplified by lowering the platform frequency from 30 cycles to 20 cycles.

cardiovascular forces,[2] it has been found that the significant qualitative notch pattern usually found in aortic insufficiency may be lost in the acceleration record if δ is kept at 6 or higher. The notching of the acceleration J peak seems to be present in nearly all cases of aortic insufficiency and may prove to have great clinical significance in the future. We have found that the distinctive acceleration notched J pattern associated with aortic insufficiency can better be seen if $\delta = 4$. Fig. 8 illustrates this point; the acceleration curves are for the same person shown in Fig. 7, who was re-examined two months after the tracing in Fig. 7.

By lowering the platform frequency from 30 c.p.s. to 20 c.p.s., the frequency ratio δ was changed from 6 to 4. This is easily accomplished by adding approximately two pounds of weight to the platform on the legs. It can readily be seen that the J′ notching is of greater amplitude. The effect of frequency parameter

on the acceleration response is further shown in Fig. 9. This figure is based on an analytical evaluation of the two-degree-of-freedom system, in which the body damping was taken as 0.4 of critical damping and damping of the skin 0.2 of critical damping. It can readily be seen from an examination of this figure that for frequency components above 80 per cent of body frequency ($\beta > 0.8$) the lower the value of δ, the greater the amplification.

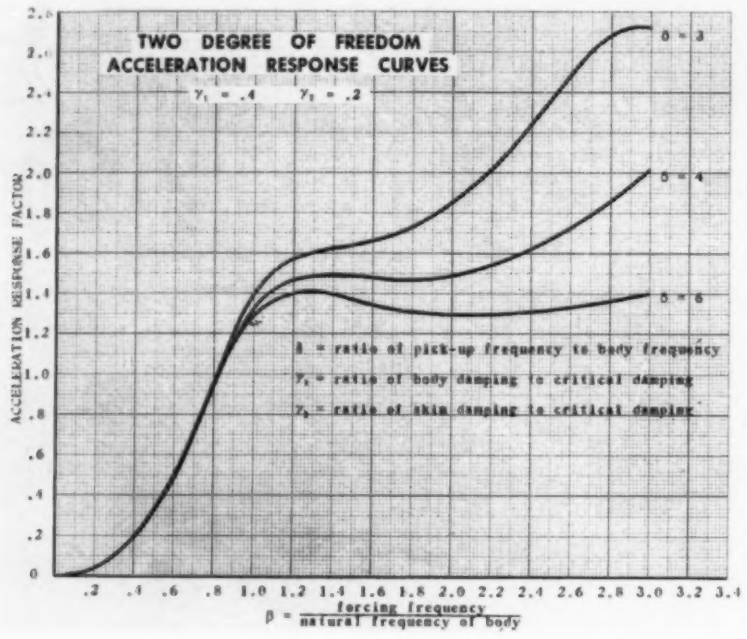
TWO DEGREE OF FREEDOM
ACCELERATION RESPONSE CURVES
γ1 = .4 γ2 = .2
δ = 3
δ = 4
δ = 6
ACCELERATION RESPONSE FACTOR
β = ratio of pick-up frequency to body frequency
γ1 = ratio of body damping to critical damping
γ2 = ratio of skin damping to critical damping
β = forcing frequency / natural frequency of body

Fig. 9.—Acceleration response for complete ballistic system demonstrating attenuation of frequency components below 80 per cent of the body natural frequency and amplification above this value.

SUMMARY AND CONCLUSIONS

1. Normal standards for displacement, velocity, and acceleration ballistocardiographs found in direct ballistic measurements are presented in fifty normal adults.

2. The techniques for measurement of body motion approximating the single degree of freedom response have been discussed.

3. Comparisons of ten cases of aortic insufficiency have shown that the deviations from normal are usually (1) higher amplitude on all measurements, (2) deeper velocity K waves, and (3) higher amplitude acceleration K wave, especially when measured from the base line and usually notching of the acceleration J peak with the ratio of J to K peak over 1.3.

4. Fourier analysis shows that the notching of the acceleration J peak previously believed to be associated with high-frequency (above 15 cycles) components of the ballistic record are actually the result of phase shift associated with lower frequency components (below 10 cycles).

5. Methods of taking advantage of the nonlinear response characteristic of the acceleration ballistocardiograph to bring out important notch patterns are discussed.

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FACTORS AFFECTING THE LOW-FREQUENCY, CRITICALLY-DAMPED BALLISTOCARDIOGRAM, WITH SPECIAL REFERENCE TO AGE, BODY SIZE, AND BODY COMPOSITION

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THE low-frequency, critically-damped ballistocardiograph[1] has not received as much attention as the high-frequency bed of Starr and associates[2] or as the body pickup devices introduced by Dock and Taubman.[3] Numerous studies have been reported attempting to define the usefulness of the latter two ballistocardiographic (BCG) methods in assessing the status of the cardiac patient. The current knowledge regarding these methods has been described in two recent reviews[4,5] and a monograph.[6]

The fact that the low-frequency ballistocardiographic pattern assumes atypical forms in the presence of degenerative heart disease has been noted by Mathers and associates.[7] Quantitative comparisons have been made of ballistocardiographic forces of apparently normal individuals and patients with hypertension[8] and with patients with arteriosclerotic heart disease.[9] In general, the differentiation between apparently normal individuals and those with cardiac disease has been somewhat disappointing.

However, no attempt has been made to systematically examine the several items of force and time in the ballistocardiographic pattern to determine sources of variation and to lay the ground work for the construction of normal standards which may be used to evaluate the effectiveness of the low-frequency ballistocardiogram in differentiating the healthy individual from the cardiac patient. Since one must know whether the ballistocardiogram differentiates one man from another, data will be presented to define the reliability of the several BCG measurements. The sources of variation which will be examined are pulse rate, blood pressure, age, body size, and the amount of body fat.

The low-frequency ballistocardiograph was originally designed for the purpose of estimating the cardiac output from measurements of the I and J

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waves.[10] Comparisons of cardiac output determined by the BCG and the acetylene procedure corrected to direct Fick values in this laboratory have shown that in normal individuals of widely varying body composition, the BCG gives only a rough approximation of the cardiac output and that in the presence of hemodynamic disturbances produced by norepinephrine both the direction of change and the absolute magnitude are incorrectly indicated.[11] In addition, Cathcart and associates[12] have reported that in the population found in hospitals there is no correlation between the cardiac output determined by the direct Fick (catheter) method and that calculated from the ballistocardiogram. Emphasis, therefore, has been placed on the force and time measurements found in the ballistocardiogram rather than the calculated cardiac output.

SUBJECTS AND CONDITIONS

The subjects were recruited from university students and local businessmen. Group I was made up of eighty-three clinically healthy university students, 18 to 21 years of age. Groups II and III were composed of 186 businessmen whose ages ranged from 49 to 58 years. These men were selected from a larger group of 274 men of the same age who have been under study in this laboratory for five successive annual examinations at the time of collection of the ballistocardiographic records. This made it possible to classify the subjects with regard to their cardiovascular status more precisely than is ordinarily feasible. Group II consisted of 127 men who during the preceding five years had not had a blood pressure above 140/90 mm. Hg, had not had an abnormal electrocardiogram either at rest or after exercise, had not complained of pain in the chest or discomfort during exercise, and who had a normal heart size by radiologic criteria. Satisfactory data were available on the per cent of fat in the body for 114 of these men. This group was further subdivided into sixty-nine men who had ballistocardiographic wave forms which were typical of those found in young men and forty-five who had atypical ballistocardiographic wave forms. Group III was made up of fifty-nine men whose blood pressure had been recorded above 140/90 mm. Hg but only occasionally over 150/100. None of these men had important eye ground changes or electrocardiographic evidence of left heart strain. Group III was further subdivided into men who had typical ballistocardiographic patterns (IIIa $N = 35$) and those who had atypical pattern (IIIb $N = 24$). Because of incomplete data these last two groups were cut to thirty-two (IIIa) and twenty-two (IIIb) when percentage fat was used in calculations. Group IV was made up of Groups IIa and IIIa and Group V was made up of Groups IIb and IIIb. The remainder of the 274 men were not included in the analysis because of the following considerations: (1) patterns too distorted to attempt measurement ($N = 9$); (2) miscellaneous conditions such as tremor, diabetes, valvular lesions, etc. ($N = 21$); (3) abnormal electrocardiograms ($N = 21$); (4) hypertension ($N = 8$); (5) myocardial infarctions ($N = 7$); (6) incomplete data, failure to obtain records due to instrumentation failure, etc. ($N = 35$).

The subjects reported to the laboratory in the morning without breakfast. They rested 20 minutes on a bed while a blood sample was taken, a short history obtained, and a physical examination performed. After this the subjects walked

to the next room where the ballistocardiogram was recorded 5 minutes after lying down on the BCG bed. After the ballistocardiogram, a resting electrocardiogram was obtained, and the subject then walked for 15 minutes on a motor-driven treadmill at 3 m.p.h. on a 5 per cent grade. An electrocardiogram was obtained between 1 and 2 minutes of recovery. Body densities were determined with the water immersion method after all functional measurements had been carried out.

METHODS

The ballistocardiograms were obtained with the use of the apparatus described by Nickerson and associates.[10] Records were taken with the simultaneous recording of heart sounds and also of respiration as indicated by a thermocouple placed just in front of the subject's nose. Records were taken during quiet respiration and during apnea at the mid-respiration point. The bed was calibrated for every record with a 50 gram weight during breath holding at full inspiration. In selected groups of subjects both the breath-holding and breathing records were analyzed but in general the majority of the records were only measured during quiet breathing. Measurements were carried out on ten consecutive complexes during quiet respiration and on four consecutive complexes during apnea.

Body density measurements were made by the immersion method and included a determination of the volume of air in the lungs at the time of underwater weighing.[15] Details of the densitometry and electrocardiographic procedures have been reported elsewhere.[13-16]

RESULTS

The Reliability of the Ballistocardiograph.—Since an important source of variability may reside in the instrument, it is important to have a measure of the repeatability of successive measurements close together in time on the same individual. Two BCG records were taken on thirty individuals selected at random from the middle-aged group. The time interval between records was three to five minutes. The coefficient of reliability between the first and second trials was found to be 0.86. The data, which are plotted in Fig. 1, show that there is a tendency for the second IJ force to be smaller than the first. This can be attributed to failure to attain completely basal conditions during recording. The true instrumental variation was somewhat smaller than that indicated by the standard error of measurement which was found to be 3.85 grams or 10.3 per cent of the mean, which in this group was 37.5 grams.

An important source of the instrumental variability was found to be in the calibration. The correlation coefficient between the displacement in millimeter per gram of calibrating weight on successive records was 0.96. The standard error of measurement was 5.3 per cent of the mean displacement value. Thus it appears that calibration errors may account for as much as 50 per cent of the variability in the measurement of the IJ force.

The instrumental variability is small enough so that we may be sure that the ballistocardiogram differentiates one individual from another. However, successive measurements separated by short time intervals do not give any information on whether ballistocardiographic characteristics are stable over a period of time. The test-retest coefficient of reliability between records taken a year apart on the same group as reported here was found to be 0.87. Further information on this point was obtained from twenty-three men selected (for another purpose) from Group II by applying the analysis of variance technique to data from ballistocardiographic records taken on three successive occasions one year apart. The results are presented in Table I. It will be noted that a significant distinction is made between individuals and that there is no significant

trend between years in all the ballistocardiographic items studied. It is clear that the ballistocardiographic forces and derived functions are stable characteristics of the individual over periods of at least 2 years.

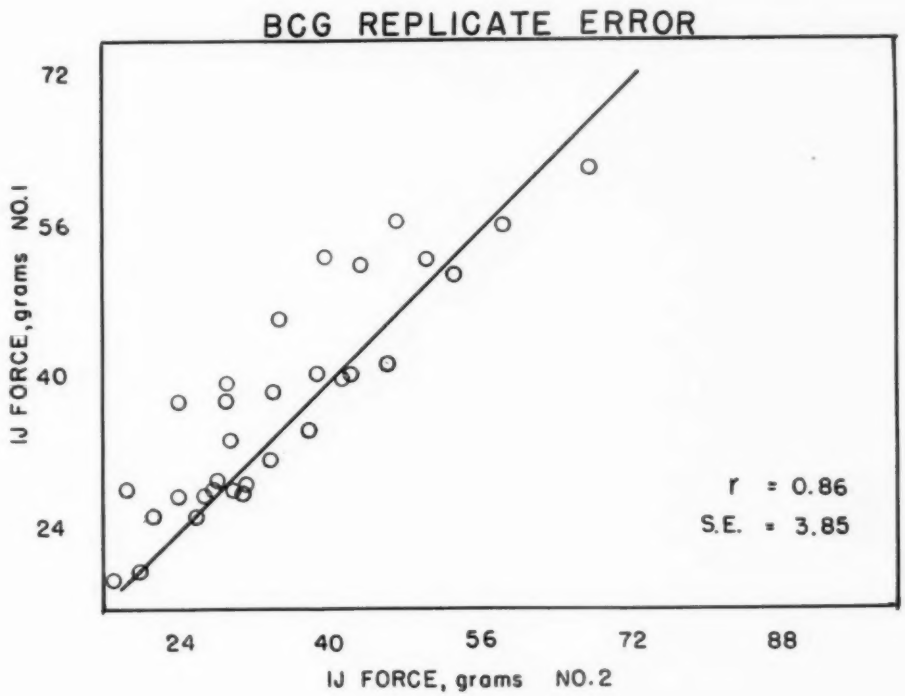

Fig. 1.—Scatter plot of duplicate determinations of IJ force on thirty individuals. The second determination followed the first within five minutes. The line gives the position of identical determinations.

TABLE I. RESULTS OF ANALYSIS OF VARIANCE OF HI FORCE, IJ FORCE, AND APPARENT STROKE VOLUME RECORDED ON THREE OCCASIONS ONE YEAR APART IN A GROUP OF TWENTY-THREE CLINICALLY HEALTHY MIDDLE-AGED BUSINESSMEN

		BREATHING			BREATH-HOLDING		
		HI FORCE	IJ FORCE	STROKE VOLUME	HI FORCE	IJ FORCE	STROKE VOLUME
Per cent of population variance attributed to	(a) Inter-individual variability	60.9	72.6	69.4	55.5	60.7	47.0
	(b) Year-to-year variability	−1.1	−0.3	−0.2	3.1	−0.7	−1.1
	(c) Random error	40.2	27.7	30.8	41.4	40.0	54.1
F tests	Between individuals	5.55*	8.87*	7.75*	5.02*	5.55*	3.60*
	Between years	0.38	0.72	0.87	2.74	0.56	0.54

*Significant at 1 per cent level of probability

It is useful to set up fiducial limits for the expected variability of the IJ force from one occasion to another in a given individual. For this purpose ninety-nine men in Group IV whose records were available from 1951 and 1952 were studied. The regression equation which would predict the IJ force found in 1952 from that observed in 1951 for records with typical patterns is given below:

$$\hat{y} = 10.686 + 0.744x \quad (1)$$

where y is the expected (1952) value and x is the previously observed (1951) value. The coefficient of reliability was 0.74 and the standard error of measurement was 4.78 grams. So we may say that over a period of a year, the IJ force of a middle-aged individual would not change more than 9.56 grams in 95 occasions out of 100.

The corresponding prediction equation for records with atypical patterns based on seventy men for whom complete data were available in Group V is presented below:

$$\hat{y} = 12.110 + 0.630x \quad (2)$$

where y and x have the same meaning as in Equation 1. The coefficient of reliability was 0.65 and the standard error of measurement was 5.25.

Table I includes measurements made on both the breathing and breath-holding records. The percentage of the total variance ($v = \sigma^2$) accounted for by the differences between individuals is smaller in the breath-holding recordings in each item examined. Ballistocardiographic forces estimated from breath-holding records do not differentiate between individuals as precisely as those obtained from breathing records. Numerous other authors have made observations which support the concept that cardiac function during breath-holding is quite variable depending on the position of the diaphragm,[12] the level of the intrathoracic pressure,[17] and other pulmonary factors. It is for this reason that the data to be discussed below are taken exclusively from breathing records.

TABLE II. AGE AND ANTHROPOMETRIC CHARACTERISTICS OF THE SEVERAL GROUPS OF SUBJECTS

	N	AGE		HEIGHT		WEIGHT		SURFACE AREA		% FAT	
		M	S.D.	M	S.D.	M	S.D.	M	S.D.	M	S.D.
Group I	83	23.2	2.3	176.6	6.8	73.8	13.5	1.90	0.18	12.3	7.8
Group II	127	53.3	2.8	175.4	6.1	75.0	10.1	1.90	0.14	23.9	6.4[1]*
Group IIa	69	52.8	2.6	175.0	5.9	74.4	9.9	1.89	0.14	23.7	6.3
Group IIb	50	53.8	3.1	176.4	6.2	76.7	10.0	1.93	0.14	24.2	6.5[2]*
Group III	59	53.0	2.8	175.7	6.1	83.4	11.6	2.00	0.15	28.6	5.3[3]*
Group IIIa	35	52.8	2.7	176.2	6.2	84.6	11.0	2.01	0.15	28.5	5.3[4]*
Group IIIb	24	53.2	3.0	175.1	5.8	81.5	12.4	1.97	0.15	28.6	5.6[5]*
Group IV	101	52.7	2.6	175.4	6.0	77.5	11.0	1.93	0.15	25.2	6.4
Group V	67	53.5	2.9	175.8	6.0	78.6	11.1	1.94	0.15	25.6	6.5

Group I consisted of clinically healthy young university males; Group II of normotensive middle-aged businessmen; Group III of middle-aged men who had blood pressure elevations above 140/90 mm. Hg but were not consistently over 150/100; Group IV of all men in Group II and III who had typical BCG patterns and Group V of all men in Groups II and III who had atypical BCG patterns. Group II and Group III are further broken down into men who had typical BCG patterns (a) and men who had atypical patterns (b).

*Incomplete data on body composition necessitated reducing groups to following numbers for per cent fat column: (1) N = 114, (2) N = 45, (3) N = 54, (4) N = 32, (5) N = 22.

Age and Ballistocardiographic Measurements.—The mean ages and anthropometric characteristics of several groups of individuals together with the values of N are presented in Table II. The young and middle-aged groups differed by approximately thirty years. The normal, middle-aged men (Group II) were close to the same weight and height as the young men. The principal

TABLE III. MEANS AND STANDARD DEVIATIONS OF THE BALLISTOCARDIOGRAPHIC ITEMS MEASURED ON THE SEVERAL GROUPS OF SUBJECTS

	N	HI FORCE		IJ FORCE		IJ TIME (SEC.)		HJ TIME (SEC.)		IJF / IJT		IJF / IJT (PULSE)		IJF (PULSE)		CARDIAC INDEX	
		MEAN	RANGE	M	S.D.	M	S.D.	M	S.D.	M	S.D.	M	S.D.	M	S.D.	M	S.D.
Group I	83	20.01	4.0–59.1	51.8	15.3	0.14	0.013	0.23	0.019	356	90	23.0	6.6	3.35	1.10	3.42	0.89
Group II	127	9.42	0.0–25.9	37.0	9.2	0.13	0.013	0.19	0.019	284	64	17.4	4.3	2.26	0.57	2.62	0.67
Group IIa	69	10.75	3.3–22.2	39.3	9.0	0.13	0.011	0.20	0.017	299	64	18.0	4.4	2.35	0.58	2.70	0.67
Group IIb	50	7.29	0.6–26.0	33.6	8.8	0.13	0.013	0.19	0.018	260	59	16.9	4.2	2.16	0.56	2.50	0.67
Group III	59	6.89	0.0–18.2	33.0	10.2	0.12	0.014	0.18	0.023	270	68	17.4	5.0	2.12	0.72	2.66	0.79
Group IIIa	35	8.07	1.0–18.2	36.5	10.3	0.12	0.012	0.19	0.021	290	70	18.4	5.3	2.32	0.74	2.77	0.82
Group IIIb	24	5.16	0.0–13.2	27.7	7.6	0.12	0.016	0.17	0.022	241	54	16.0	4.4	1.84	0.60	2.51	0.75
Group IV	101	9.96	1.0–22.2	38.3	9.6	0.13	0.014	0.20	0.020	295	67	18.1	4.7	2.34	0.64	2.72	0.72
Group V	67	6.63	0.0–26.0	31.7	8.9	0.12	0.015	0.18	0.021	253	59	16.4	4.2	2.04	0.59	2.47	0.69

For the description of the groups see Table II.

difference in anthropometric characteristics was in the per cent of body fat which was almost twice as large in the middle-aged group as in the young men. This difference has been discussed in detail elsewhere.[15] The subjects in Group III who had higher blood pressures were generally heavier and fatter than the men in Group II. The means and standard deviations for the principal force and time characteristics of the BCG record are presented for the several groups in Table III. The distribution of the several measurements was found to approximate a normal distribution curve with the exception of the HI force which was badly skewed. Standard deviations for HI force are not presented. Both times and forces decreased with age, and the decreases were highly significant when tested with the conventional *t* test.

The largest decrements with age occurred in the HI force means which declined 47 to 63 per cent in the several groups of middle-aged men. The IJ force decreased from 24 to 47 per cent with the IJ slope and the slope x pulse showing somewhat smaller decreases (16 to 32 per cent).

The differences between the young and middle-aged groups in the IJ and HJ times were from 0.01 to 0.02 second in the former (7 to 14 per cent) and 0.03 to 0.06 second (13 to 26 per cent) in the latter. It follows that the important shortening of time in the BCG pattern occurred in the HI time which was 0.09 second in the young men and varied between 0.06 and 0.07 in the older groups.

The effects of age on the time intervals between the first heart sound and the several BCG waves were studied by comparing data from thirty-three young men with that from twenty-three middle-aged men selected from Group IIa. The time from the beginning of the first heart sound to the peak of the H wave in the young group was 0.083 ± 0.017 second while that of the middle-aged group was 0.078 ± 0.017 second. The difference of 0.005 second is not statistically significant.

It will be pointed out below that the body dimension which appears to be the most consequential factor influencing the IJ force is the height. It is useful then to determine the size of the age decrement between young and middle-aged groups which have been matched for height.

Men were eliminated from the young group of eighty-three until the mean height exactly matched that of Group IIa. The two groups are compared in Table IV. The decrease in the IJ force was 23 per cent, which is only slightly smaller than the difference found in the unmatched group. The same relation held in the derivatives of the IJ force and in the HI force comparisons. The *t* tests listed in Table IV show that these differences are highly significant.

TABLE IV. EFFECTS OF AGE ON BALLISTOCARDIOGRAPHIC MEASUREMENTS

	HEIGHT (CM.)	% FAT	WEIGHT (KG.)	HJ TIME (SEC.)	IJ TIME (SEC.)	HI FORCE	IJ FORCE	IJF / IJT	IJF / IJT (PULSE)
Young men	174.95	12.75	73.0	0.228	0.144	19.57	51.0	351	22.6
Middle-aged men	174.95	23.66	74.4	0.200	0.131	10.75	39.3	299	18.0
△	0.00	10.91	1.4	0.029	0.013	8.82	11.7	52	4.6
△ in %				12.3	9.0	45.0	22.9	14.8	20.4
t-test value*				9.27	5.14	8.09	5.45	3.95	4.95

The group of young men was made up of seventy-two individuals whose heights were matched to those of sixty-nine middle-aged men. The mean age of the young men was 23.4 years and that of the older men was 52.8 years.

*A *t*-test value of 2.61 indicates that the observed difference wou'd occur by chance on one occasion in 100.

It is clear that the mean age difference of approximately 30 years results in a decrease in the principal force measurement, i.e., an IJ force decrement of not less than 23 per cent. This difference can be increased to as much as 46 per cent in Group IIIb by the presence of atypical ballistocardiographic forms in the sample and by the number of individuals who have had a history of elevated blood pressure.

The Relationship Between Ballistocardiographic Items and Measures of Body Size in Young Men.—Correlation coefficients between measures of body size and BCG items related to force are presented in Table V. The largest correlation coefficients were found between BCG force items (IJ force, IJ force x pulse, IJ force / IJ time, and stroke volume) and surface area. Correlation coefficients between weight and force items were slightly smaller while those between height and force items were the smallest. In fact the only correlation coefficient that was not significantly different from zero was that between stroke volume and height. Fisher's z transformation was employed to test the significance of the difference between the several correlation coefficients, and it was found that the correlation coefficients relating force and surface area were significantly larger than those relating height and force. Although there is no real difference between surface area and weight as reference points for the construction of standards, the surface area may be preferred for theoretical reasons.

TABLE V. CORRELATION COEFFICIENTS BETWEEN BALLISTOCARDIOGRAPHIC MEASURES OF FORCE AND TIME AND COMPONENTS OF BODY SIZE IN CLINICALLY HEALTHY YOUNG MEN

	FORCES, N = 83				TIME INTERVALS, N = 33					
	IJ FORCE	$\frac{\text{IJF}}{\text{IJT}}$	(IJF)xP*	STROKE VOL.	SH	SI	SJ	HJ	HI	IJ
Ht.	0.33	0.32	0.35	0.19	0.18	0.34	0.49	0.49	0.28	0.54
Wgt.	0.43	0.43	0.45	0.38	0.16	0.06	0.22	0.14	−0.11	0.37
S. A.	0.46	0.45	0.48	0.38	0.20	0.15	0.34	0.26	−0.03	0.47

The correlation coefficients with forces were calculated on data obtained from single records in eighty-three subjects while the correlation coefficients with the time intervals were computed using the means of measurements made on four separate records for each of thirty-three subjects. SH, SI, etc., indicate the time interval between the beginning of the first heart sound and the designated ballistocardiographic wave.

*Pulse

The significance of the correlation coefficients at

	5%	1%
for N = 33	0.34	0.44
N = 83	0.21	0.29

The relationships between body size and time intervals were investigated in a subgroup of thirty-three young men. Ballistocardiograms were obtained on these men on four occasions. Time intervals for each man were averaged and used to compute the correlation coefficients presented in Table V. Time intervals between the beginning of the first heart sound and the peak of the ballistocardiographic waves are indicated by SH, SI, etc. The use of averages of time intervals for individuals in this group had the advantage of reducing the variability due to random errors of measurement, particularly between the first sound and the peak of the ballistocardiographic waves.

The largest correlation coefficient in Table V is that between IJ time and height. The intervals which do not include the IJ time show either no significant correlation coefficient or at best a very low value (SI time). Weight is unrelated to any time interval except the IJ time and here the correlation is poor. This relationship may be explained in part by the association between height and weight. The second correlation coefficient which is of some importance is that between surface area and IJ time. This correlation coefficient is not as large as that relating height to IJ time so we may suggest, although it has not been proved, that height is the most important source of variation in the IJ time that has been identified.

The Relationship Between BCG Items and Measures of Body Size in Middle-Aged Men.—Correlation coefficients relating ballistocardiographic forces and time intervals to body size in sixty-nine middle-aged men are presented in Table VI. These subjects made up Group IIa and all had typical wave patterns which were free from significant respiratory interference. The

general pattern of relationships between force and body measurements is quite different in this group from that seen in the young men. The largest correlations in the middle-aged group were between the various measures of force and height. There were no significant correlations with body weight, and the correlations with surface area were low and depend in large measure on the inclusion of height in the calculation of the surface area. The coefficients between force measurements multiplied by the pulse rate and measures of body size are all somewhat smaller than with the force measurements alone. All efforts to find multiple regression equations which would yield larger correlation coefficients than those found with height were failures with the exception of IJ force with height and per cent fat which had a multiple correlation coefficient of 0.65. The relationships between time intervals and measures of body size were similar to those found in the young men. In both groups height had the closest association with the time intervals studied. The height (body length) appears to be the best reference point to use in the construction of force or time standards for typical patterns of the low-frequency ballistocardiograph in middle-aged men.

TABLE VI. CORRELATION COEFFICIENTS BETWEEN BALLISTOCARDIOGRAPHIC ITEMS (FORCE AND TIME INTERVALS) AND COMPONENTS OF BODY SIZE IN SIXTY-NINE "NORMAL" MIDDLE-AGED MEN WITH TYPICAL BALLISTOCARDIOGRAPHIC PATTERNS

	FORCE	$\frac{\text{IJ FORCE}}{\text{IJ TIME}}$	(IJF) (PULSE)	$\frac{\text{(IJF)}}{\text{(IJT)}}$ (PULSE)	HJ TIME	HI TIME	IJ TIME
Ht.	0.63	0.54	0.53	0.40	0.48	0.32	0.37
Wgt.	0.23	0.19	0.01	−0.04	0.09	−0.02	0.16
S. A.	0.40	0.33	0.17	0.08	0.24	0.09	0.25

A correlation coefficient in this table is different from zero at the 1 per cent level of probability when r = 0.308 and at the 5 per cent level when r = 0.237.

The Relationship Between the Fat Content of the Body and Ballistocardiographic Items.—Correlation coefficients between both time intervals and force measures and fat as per cent of body weight are presented in Table VII along with the correlations between BCG items and fat-free body weight. It will be observed that in the young men there is a positive correlation coefficient between force items and fat as per cent of body weight. However, partial correlation coefficients between IJ force and percentage of fat holding surface area and weight constant were found to be −0.065 and −0.123, respectively. It is clear that the positive correlation coefficients between per cent fat and the several measures of force can be accounted for by the association between fat per cent and body weight (r = 0.73) or surface area (r = 0.62).

The relationship between time intervals and the percentage of fat in the body was investigated in the subgroup of thirty-three young men described here. Both the time intervals within the BCG wave form and the times between the beginning of the first heart sound and subsequent BCG peaks were investigated. None of the time intervals studied had any significant association with the percentage of fat in the body.

In the middle-aged men the relationships between BCG forces and percentage of fat were examined in two groups and the data are presented in Table VII. In middle-aged men with typical BCG wave forms (Group IIa) it was found that the correlation coefficients were negative and significantly different from zero. In the group of middle-aged men who had atypical wave forms (Group V), the same relationships were found. The differences between the negative correlation coefficients (forces vs. percentage fat) found in the middle-aged group and the positive correlations found in the young group were tested using Fisher's *z* transformation and it was shown that a significant difference existed in all three instances.

A further analysis was carried out in the larger groups (IV and V). The partial correlation coefficient between the per cent of body fat and the IJ force holding weight constant was found to be relatively large in both Group IV (r = 0.46) and Group V (r = 0.30). It happens that the

per cent of fat in the body is positively associated with blood pressure, r = 0.39 (Group IV) and r = 0.41 (Group V). It will be shown that the blood pressure is related with IJ force by a small negative correlation coefficient. We have, therefore, calculated the second order partial correlation coefficient relating IJ force with per cent fat while removing the effects of both weight and blood pressure. The value for this r in Group IV was found to be −0.42 and in Group V, −0.27. Finally, it should be mentioned that the percentage of fat in the body is unrelated to the pulse rate. There appears to be no question then that in the middle-aged group the IJ force was negatively associated with the per cent of fat in the body and that this negative association is independent of the effects of weight, blood pressure, and pulse rate.

TABLE VII. CORRELATION COEFFICIENTS BETWEEN BALLISTOCARDIOGRAPHIC MEASURES OF FORCE AND TIME ON THE ONE HAND AND THE PERCENTAGE OF BODY FAT ON THE OTHER

BCG ITEM	YOUNG MEN GROUP I			MIDDLE-AGED MEN				
				TYPICAL PATTERNS			ATYPICAL PATTERNS	
	N	FAT % B. WT.	FAT-FREE WEIGHT	N	FAT % B. WT.	FAT-FREE WEIGHT	N	FAT % B. WT.
IJ Force	83	0.24	0.42	69	−0.24	0.43	67	−0.31
(IJF)(pulse)	83	0.29	0.41	69	−0.26	0.10	67	−0.31
IJF/IJT	83	0.21	0.43	69	−0.17	0.33	67	−0.24
SH Time	33	0.22	—	—	—	—	—	—
SJ Time	33	0.14	0.26	—	—	—	—	—
HI Time	33	−0.21	—	69	−0.23	—	45	−0.26
HJ Time	33	−0.01	0.25	69	−0.32	—	45	−0.26
IJ Time	33	0.21	0.43	69	−0.18	—	45	−0.10

Data for typical patterns were taken from Group IIa and for atypical patterns from Group V.

Probability of r differing from zero at	1% level	5% level
when N = 67	0.31	0.24
N = 69	0.31	0.24
N = 83	0.29	0.21
N = 33	0.44	0.34
N = 45	0.38	0.29

The correlation coefficients between BCG force items and the fat-free body weight are included in Table VII for the sake of completeness. They are of interest only in that the fat-free body weight does not appear to have any advantage as a reference point for the construction of standards.

The Relationship of Ballistocardiographic Forces With Blood Pressure and Pulse Rate.—The association between blood pressure and BCG forces was studied in Group IV which is made up of 101 individuals who had typical BCG wave forms and a wide range of blood pressure. The blood pressure range as observed while the subject was lying on the ballistocardiograph was from 100/60 to 164/94 mm. Hg. This is a moderate range and does not include anyone who can be considered to have hypertensive disease by recent standards.[18] The systolic and diastolic blood pressures were averaged and divided by two, and the correlation coefficients were calculated with this number. In the combined group the correlation coefficient between the average blood pressure and the IJ force was −0.24. While this figure is significantly different from zero, the association between IJ force and blood pressure only accounts for 6 per cent of the total variance of the IJ force, so we may conclude that in this range of blood pressure, the effect of blood pressure on the IJ force is, for practical purposes, negligible. In addition, the correlation coefficient between the slope of the IJ limb (IJF/IJT) and average blood pressure was not significantly different from zero. Nickerson and associates[10] concluded that the square root of the average blood pressure

was the most satisfactory expression to use to correct the IJ force for the influence of blood pressure. However, correlation coefficients between the square root of the average blood pressure and IJ force as well as the slope of the IJ limb were virtually identical with those found with the average blood pressure.

Inspection of Table III shows that blood pressure had a definite influence on the means of the IJ force. The mean IJ force of Group II was significantly higher (when examined with the *t* test, $P < 1$ per cent than that of Group III. On the other hand, the means of the slope of the IJ limb in the two groups were not different nor were the means of the IJ force x pulse rate or slope x pulse rate. In both young (Group I) and middle-aged men (Group IIa) no significant correlation was found between pulse rate and measures of ballistocardiographic force.

The Effects of Atypical Ballistocardiographic Wave Forms.—Inspection of Table III shows that the important difference between groups with typical BCG wave forms and groups with atypical BCG wave forms occurs in the means of the several measures of force. The differences between the means were tested for significance with the conventional *t* test and the results are presented in Table VIII. The IJ force showed large and important differences in both Groups II and III. These differences became smaller and lost significance in Group II when the IJ force was multiplied by the pulse rate. However, there was still a significant difference in this variable in Group III. The slope of the IJ limb also gave similar results.

TABLE VIII. SIGNIFICANCE OF DIFFERENCE BETWEEN MEANS OF GROUPS MADE UP OF SUBJECTS WITH TYPICAL AND ATYPICAL BALLISTOCARDIOGRAPHIC WAVE FORMS

BCG ITEM	*t* VALUE FOUND FOR GROUP IIa VS. IIb	SIGNIFICANCE	*t* VALUE FOUND FOR GROUP IIIa VS. IIIb	SIGNIFICANCE
IJ Force	3.376	>0.1%	3.573	>0.1%
IJF/IJT = (Slope)	3.311	>1 %	2.877	>1 %
(IJF) (pulse)	1.799	<5 %	2.630	>2 %
(IJF/IJT) (pulse)	1.372	<5 %	1.779	<5 %

The probabilities were obtained with the conventional *t* test. The means and standard deviations of the several groups are presented in Table III.

The relationship between measures of body size and the BCG forces was studied in the sixty-seven men on whom complete data were available in Group V. No significant correlation coefficients were found between any measure of force [IJF, IJF/IJT, and (IJF) (pulse)], and either surface area or weight. However, the IJ force was related to height by a correlation coefficient of 0.30 (significant at the 1 per cent level of probability) while the slope of the IJ limb (IJF/IJT) was related to height by a correlation coefficient of 0.25 (significant at the 5 per cent level of probability). Neither the (IJ force) (pulse) nor the (IJF/IJT) (pulse) was related to height in this group. It is clear that atypical ballistocardiographic records are characterized by lower force values and smaller associations with other variables than ballistocardiograms which have patterns typical of healthy young men.

The Problem of Standards for the Low-Frequency Critically-Damped Ballistocardiograph.—The experimental design used here has severe limitations when the data are used to construct standards. Thus it is not possible to give reasonable values for a wide age range in males, and no data has been obtained for women. It is necessary to present standards for two separate decades. While this presentation is forced by the experimental design, it is quite possible that the proper method of setting up standards is to construct separate regression equations for each decade rather than a single multiple regression equation which combines both age and standard reference points. The value of height as a reference point changes with age if one considers the IJ force alone. Height and IJ force were associated by a correlation coefficient of 0.33 in young men and 0.63 in the middle-aged group. When tested with Fisher's *z* transformation, the difference between these two r's was found to be significant at the 2 per cent level of probability. In addition, it will be

remembered that the IJ force, the slope of the IJ limb, and the measures multiplied by the pulse rate were associated positively with the percentage of fat in young men and negatively in the middle-aged men. The differences between these several correlation coefficients in the two age groups were found to be significant. It is clear then that the relationship between both body dimensions and composition changes with age. It is not possible to prove beyond doubt that new reference points should be employed in different age groups, since in the data at hand, it could not be demonstrated that there was a significant difference in the association between reference points (height, weight, or surface area) and force measures within a single age group. However, at this stage, it seems that separate standards for each decade would be the safest procedure.

In young men, the largest correlation coefficients between force items and body dimensions were found with surface area. Efforts to improve the zero order correlations by the use of multiple regression equations all failed to produce larger coefficients. The following equations are presented with surface area as a reference point in spite of the fact that it is not possible to prove that surface area was a significantly better reference point than weight or height:

$$\text{IJ Force} = 39.72\ \text{S.A.} - 23.62 \quad (3)$$
Standard error of estimate = 13.60

$$\text{IJF/IJT} = 229.64\ \text{S.A.} - 79.92 \quad (4)$$
Standard error of estimate = 80.15

$$\text{(IJF) (pulse rate)} = 3.00\ \text{S.A.} - 2.34 \quad (5)$$
Standard error of estimate = 0.97.

Standards for middle-aged men must be set up for two separate groups, i.e., those with typical BCG wave forms and those with atypical wave forms. In Group IV it was found that height was apparently the best reference point for measures of BCG force. In general, the association between height and force measures was significantly greater than that with weight but only numerically larger than that with surface area. Attempts to find combinations of reference points which were superior to height were failures. Thus height combined with surface area, weight, or per cent of fat failed to give correlation coefficients that were significantly larger than that obtained with height alone. In addition to combinations of measures of body size and composition, the additional factors of pulse rate and blood pressure were also examined in combination with measures of body size. No advantage over height was found in any of these combinations. Standards for middle-aged men with typical BCG wave patterns then should be based on height. The following regression equations based on Group IV are presented:

$$\text{IJF} = 0.879\ (\text{Ht.}) - 115.94 \quad (6)$$
Standard error of estimate = 8.01
r = 0.55

$$\text{IJF/IJT} = 5.549\ (\text{Ht.}) - 678.41 \quad (7)$$
Standard error of estimate = 57.71
r = 0.50

$$\text{(IJF) (pulse)} = 0.052\ (\text{Ht.}) - 6.85 \quad (8)$$
Standard error of estimate = 0.56
r = 0.49

where height (Ht.) is expressed in centimeter, IJF in grams, and the IJ slope in Gram/second. For the sake of completeness, the following multiple regression equation (based on Group IIa) combining height and per cent of fat in the body is presented:

$$\text{IJ force} = 0.93\ (\text{Ht.}) - 0.23\ (\%\ \text{fat}) - 118.26 \quad (9)$$
Standard error of estimate = 6.87
r = 0.65.

In the middle-aged group, roughly 40 per cent of the subjects had some form of abnormality of wave form. It is apparent that separate standards should be provided for this group. The

correlation coefficients between measures of body size (and composition) and the IJ force were significant (Group V) but small in the case of height and body fat. Only a small advantage is obtained by using height as a reference point:

$$IJF = 0.43\ (Ht.) - 44.78 \qquad (10)$$

Standard error of estimate = 8.41.

However, the multiple regression equation including both height and per cent of fat in the body gives a correlation coefficient between observed and predicted values of 0.42. The equation is as follows:

$$IJF = 0.41\ (Ht.) - 0.39\ (\%\ fat) - 30.32 \qquad (11)$$

The standard error of estimate = 8.05.

DISCUSSION

Data on the effects of age on the low-frequency critically-damped ballistocardiographic times and forces have been presented previously by Jones[9] and Jones and Goulder.[8] Precise comparisons with the work reported here are difficult because the groups were small, the age range within groups very large, and the groups contained both males and females. However, the data of these authors clearly demonstrated decreases with age in ballistocardiographic times and forces which are roughly comparable with those reported here.

The relationship between age and ballistocardiographic forces and derived functions recorded by the high-frequency bed of Starr has been carefully studied in several laboratories. Starr and Schroeder[20] were the first to point out that ballistocardiographic forces decrease with age. Tanner[21] used these and other data to construct normal standards and gave regression equations describing the decrease of the calculated cardiac output with age. Scarborough and associates[19] studied 369 apparently normal individuals whose ages were between 22 and 69. The equation given by these authors for the regression of IJ amplitude on age for men can be used to compare the decrease in the IJ force with age recorded by the two types of equipment. Scarborough's regression equation was based on 165 BCG records with normal patterns taken on men whose blood pressures were less than 140/90 mm. Hg. This equation states that between the ages of 23 and 53 the IJ amplitude decreased 28 per cent. This may be compared with the difference in IJ force between Group I and IIa of 24 per cent. Thus it appears that the low-frequency ballistocardiograph measures a decline with age of the IJ force which is roughly of the same order of magnitude as that of the high-frequency machine. Since there is reason to believe that the IJ force of the two instruments does not have exactly the same physical dimensions, more precise comparisons are not justified.

The change in the importance of height as a reference point with age raises an interesting question regarding the aorta. One may ask whether in the middle-aged man the length of the aorta is not actually the important determining factor of the IJ force and whether this is so in the middle-aged groups because of changes in the hemodynamics related to aging of the aorta. It seems reasonable to suggest that the increase in the apparent pulse wave velocity with age may well play an important role here.[22]

Scarborough and associates[19] carried out a careful study of the factors which may be used as reference points for setting up standards for the high-frequency

ballistocardiogram. These authors found that the IJ force was not related to any of the common measures of body size including height, weight, and surface area. Tanner's data,[21] which were confined to calculated stroke volumes and cardiac outputs, gave correlation coefficients for relationships with height, weight, and surface area which were not significantly different from zero. It is apparent that from the available data the low-frequency ballistocardiogram differs from the high-frequency ballistocardiogram in that correlations have been found between low-frequency ballistocardiographic forces and measures of body size which allow one to set up more accurate standards. This allows a reduction of the scatter of values around the predicted value by as much as 50 per cent. It is tempting to conclude that associations which were found between the low-frequency ballistocardiogram and measures of body size were not found in the case of the high-frequency ballistocardiogram because of differences in the design of the instrument. Indeed, evidence has recently been presented[23] to demonstrate that the low-frequency critically-damped ballistocardiograph, although not a perfect recorder, causes less distortion of imposed force than the high-frequency instrument. However, conclusions regarding instrumentation cannot be drawn by comparison of work done in this laboratory with that of Scarborough and associates[19] or Tanner[21] since the low-frequency machine was studied with men in the fasting state and the high-frequency instrument was studied with subjects who were not fasting. The effects of meals[24] are large in the case of the high-frequency instrument and, in a series of records obtained at random times after meals, could well erase any relationship with body size.

In contrast to the experience with measures of force, time intervals such as duration of the I and J waves in the high-frequency ballistocardiogram resemble the time intervals of the low-frequency ballistocardiogram in that they are related to height, weight, and surface area.[19]

The correlations between IJ force and per cent of fat in the body are of cons'derable interest, since a priori it may be argued that the transmission of force through tissues encased in a large amount of fat would be less efficient than through tissues whose composition was normal. The negative correlation coefficient between IJ force and per cent of body fat in the middle-aged man suggests such a possibility in this age group. An alternate explanation is that in the older obese individual the acceleration of blood by the heart is slower than it is in his thin contemporary. This interpretation is consistent with the concept that obesity causes cardiac damage, a thesis that has been supported by many arguments.[25] A small contributing factor to this negative correlation of IJ force with per cent of body fat is the increasing A-V oxygen difference that has been observed with increasing proportion of body fat.[26] Finally, one may argue that since increased body fat is not a demonstrably poor transmitter of cardiac force in the young man, the decrease in the IJ force with increasing body fat content in the older individual is due to a decrease in the original force. But this argument carries with it the dangerous assumption that the process of aging does not influence the elastic properties of fat and fat-infiltrated tissues.

The effect of age on the ballistocardiogram cannot be completely evaluated until the possible contribution of body fat has been considered. The possibility

that cardiac force is lost in transmission through fatty tissues whose force transmission characteristics have changed can be examined in the following manner. The original cardiac force is generally considered to be the product of mass and acceleration. It is conceivable that the heart would lose some of its capacity to accelerate blood with passing time; by the same token, it is not likely that it would increase it. Cardiac outputs and ballistocardiograms carried out as close together as possible on the same individuals selected from Group I and IIa have been reported elsewhere.[11] The ratio of the ballistocardiographic output to that by the corrected acetylene method in the young men was found to be 1.17 and in the middle-aged group 1.0. So it appears that there was less force recorded in the middle-aged group per unit of cardiac output but that the loss was not large. This loss could be due to either loss of capacity to accelerate blood by the heart muscle or it could be due to a change in the manner of transmission of force from the heart to the table. In either case, the change is not a large one.

The age trend in the force measurements reported here may possibly have some value in population comparison studies of the type initiated by Keys.[27] In carrying out such studies, care will have to be taken to make comparisons between segments of the population matched for height, per cent fat, blood pressure, and ballistic pattern as well as comparisons between complete samples of the populations under study.

SUMMARY AND CONCLUSIONS

1. Ballistocardiograms (BCG's) were obtained with the low-frequency' critically-damped apparatus on eighty-three clinically healthy university students and 186 businessmen, age 49 to 58 years. The young men were examined on only one occasion. The middle-aged men were seen annually for five successive years and BCG records were made on the last three occasions. In all cases, the men came to the laboratory before breakfast and rested in bed at least 20 minutes before getting on the ballistocardiograph.

2. The coefficient of reliability for the IJ force (breathing records) was found to be 0.86 in thirty clinically healthy middle-aged men whose records were taken five minutes apart. The standard error of measurement was calculated to be 10 per cent of the mean value. The random error in the calibration accounted for 50 per cent of the standard error of the IJ force. The coefficient of reliability of the IJ force obtained from records taken on the same individuals one year apart was 0.87. An analysis of variance carried out on three records taken a year apart showed that 72 per cent of the variance of the IJ force could be attributed to interindividual variability, 27 per cent to random error and less than 1 per cent to year-to-year variability. It is concluded that the IJ force of the low-frequency, critically-damped BCG is a stable characteristic of middle-aged men.

3. In young men the IJ force was found to be related to surface area with a correlation coefficient of 0.46, to body weight by 0.43, and to height by 0.33. Correlation coefficients of similar magnitude were found between these measures of body size and the slope of the IJ limb, the calculated stroke volume, and the IJ force multiplied by the pulse.

4. Correlation coefficients between components of body size and measures

of ballistocardiographic forces were calculated in sixty-nine middle-aged men who were clinically healthy by rigid criteria and who also had typical wave patterns. The largest correlation coefficients were consistently found between height and the ballistocardiographic forces. Correlation coefficients with weight and surface area were either small or not significantly different from zero. It was concluded that height (body length) is the best single reference point of bodily dimensions for the construction of standards.

5. The relationships between time intervals within the ballistocardiographic pattern and measures of body size were studied in a selected group of thirty-three young men and in sixty-nine middle-aged men with typical ballistic patterns. In addition the time intervals between the beginning of the first heart sound and the ballistocardiographic wave peaks were studied in the young group. In all variables studied the largest correlation coefficients were found with height.

6. In young men there was a positive correlation coefficient between IJ force (and related measurements) and the per cent of fat in the body. This was shown to be zero when the effects of weight were removed. On the other hand, in middle-aged men the IJ force (and related measures of force) had a negative correlation coefficient with the per cent of fat in the body, and it could be shown that this effect was independent of weight, height, blood pressure, and pulse rate.

7. No associations were found between pulse rate and ballistocardiographic forces in young men or middle-aged men. Small negative correlations were found between average blood pressure and IJ force in the middle-aged men. This relationship did not improve when the square root of the average blood pressure was studied.

8. The records of the middle-aged men were separated into typical and atypical patterns. It was shown that time intervals were not different between the two groups, but that the atypical groups invariably had lower force values than comparable groups with typical patterns. In addition, correlation coefficients with measures of body size were lower than in groups with typical patterns. The only exceptions to this were the correlation coefficients between per cent of fat in the body and IJ force, which were of the same order of magnitude in the two groups.

9. The effects of age were studied by comparing the young (18 to 26 years) and middle-aged (48 to 57 years) groups. The mean IJ force of sixty-nine clinically healthy middle-aged men who had typical ballistocardiographic patterns was 24.1 per cent smaller than that of eighty-three normal young men whose mean age was 30.1 years less. The decrement of the IJ force between the young men and the middle-aged groups ranged from 24 to 46 per cent depending on the number of individuals in the groups who had atypical ballistocardiographic patterns and who had elevated blood pressures. Similar results were obtained with the HI force, IJ slope, and the force measures multiplied by the pulse rate. In general, the time intervals decreased with age, the only exception being the time from the first heart sound to the peak of the H wave.

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QUANTITATIVE ESTIMATION OF VENTRICULAR STRAIN IN THE LIMB LEADS

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EXCESSIVE work performed by the ventricular musculature produces by exhaustion changes in the electrocardiogram which are known since Barnes and Whitten[1] as ventricular strain. Increased voltage of the QRS complex, flattening or inversion of the T wave in that lead where the main deflection of the ventricular complex is directed upward, or increase in height of the T wave with a downward directed main deflection, and finally changes in the course and form of the S-T segment are the most characteristic features of this frequent electrocardiographic pattern in the standard leads. Ventricular strain must be distinguished from ventricular hypertrophy, although both are frequently combined. The same cause, e.g. hypertension, that in the beginning provokes pure hypertrophy may lead to burden and so to strain, if it is excessive and of long duration. This is the commonest form of ventricular strain. When sufficiently prolonged, it is usually combined with hypertrophy of either the left or right ventricle, according to the etiologic factors. However, strain may develop in acute form on the basis of a scarcely altered or even normal ventricular musculature as in cases of acute cor pulmonale or during attacks of paroxysmal hypertension.

In the determination of the electrocardiographic aspect of ventricular strain patterns the most important factors are the position of the heart and the degree of ventricular hypertrophy and that of fatigue. The position of the heart is chiefly responsible for the distribution of electrical potential in the extremities and also for the form of the ventricular complex. On the other hand, the position of the heart is decisive for the position of the electrical axis. Ventricular hypertrophy is combined usually with conventional deviation of the electrical axis. Thus left ventricular hypertrophy causes conventionally left-axis deviation. However, according to body build the axis deviation may be absent or in cases of vertical position of the heart even right-axis deviation can be observed. This consideration is valid also for right ventricular hypertrophy. Simultaneous hypertrophy of both ventricles may counterbalance each other in such a manner that no shift in the position of the electrical axis is produced. Therefore, it remains always a complicated problem to interpret with accuracy in each case how much must be attributed to position, hypertrophy, or strain.

The electrocardiographic diagnosis of ventricular strain is based both on qualitative signs and measured data, as pointed out by Sokolow and Lyon.[2]

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Height of the QRS complex, height and direction of the T wave, form, course, and location of the S-T segment in the standard leads must be determined. The same data in addition to the relative size of the R and S wave, expressed as R/S and R/T ratios, have to be determined in precordial Leads V_5 and V_6 in cases of left ventricular hypertrophy, and in V_1 when right ventricular hypertrophy is present. As a result, conclusive knowledge is obtained concerning the presence and degree of actual ventricular strain, indeed not in exact quantitative terms but rather in an approximate way.

In the standard leads ventricular strain causes opposite changes between the QRS group and the T wave on the one hand, and between the first and third leads on the other hand. In cases of left ventricular strain, the R wave in the beginning increases in height as an expression of induced overactivity; later on, the T wave flattens and becomes inverted. Simultaneously, or somewhat delayed, the S wave in Lead III becomes deepened and the T wave increases in height. Identical changes develop in right ventricular strain where increase of the R wave and flattening and inversion of the T wave occur first in Lead III accompanied by increasing deepening of the S wave and increasing positivity of the T wave in Lead I. These changes have most regularly been noted since the earliest observations and can be considered as the basic elements of ventricular strain patterns in the limb leads.

In the present paper a new empirical formula will be introduced which expresses in a single equation the opposite changes of the QRS complex and T wave in limb Leads I and III, and which thus permit a quantitative estimation of the intensity of existing ventricular strain.

METHOD AND MATERIAL

It was found that changes of the QRS complex and those of the T wave caused by ventricular strain in limb Leads I and III can quantitatively be summarized by the equation

$$[(R_1 - S_1) - 2T_1] + [(S_3 - R_3) + 2T_3] \quad .$$

The result is a scalar quantity, a positive or negative number; as strain index it will be used to estimate the degree of ventricular strain.

In the present study the following method was used. In the conventional electrocardiogram (Sanborn) of the resting subject in recumbent position the height of the R, S, and T waves was measured in Leads I and III, and form and course of RS-T segment were determined. The sum of R_1+S_3 and S_1+R_3 was calculated in every case. Position of the electrical axis was calculated by the formula of White and Bock[3] and of Schlomka,[4] whereas the angle α was determined by means of the chart devised by Carter and associates.[5] The present paper does not deal with particularities of precordial and unipolar extremity leads: however, for purposes of a correct electrocardiographic diagnosis these leads were carefully studied in every case.

The present investigation contains observations made in a group of one hundred healthy individuals, male and female, chosen at random, fifty cardiac patients with left and thirty with right ventricular strain pattern. Each group will be treated separately.

RESULTS

Normal Subjects.—

Age: The average age was 41.8 years, with a range from 17 to 67.

Strain index: Its value was positive in sixty-four cases and negative in thirty-six cases. The calculated average of these one hundred healthy individuals was +1.84 with a standard deviation of ±5.58 and with a range from −12.5 to +12.5.

Correlation between strain index and age: Observations were classified according to increasing age in groups of 10 years, and the average value of the strain index was calculated in each of the groups. In the group of the youngest individuals, aged 11to 20 years the strain index averaged −3.5; in 21 to 30 age group, −1.21; in 31 to 40 age group, +0.85; in 41 to 50 age group, +2.1; in 51 to 60 age group, +4.32; and finally in the group of persons over 60 years the strain index averaged +7.5. It is evident that there exists a definite correlation between age and strain index; its negative value becomes increasingly positive with advancing age.

Correlation of the strain index with its composing factors: The strain index consists of two components: the QRS and T factors on the one hand and their partial values in Leads I and III on the other hand.

QRS and T factors: The QRS factor is represented in the formula of the strain index by the expressions $(R_1 - S_1)$ and $(S_3 - R_3)$. The proportion by which both components participate in the numerical determination of the index is different in the two subgroups of healthy individuals with a positive or negative index.

In the subgroup with a positive strain index the QRS factor averaged +9.03, i.e., 69.5 per cent, whereas the factor T was +3.96, that is 30.5 per cent of the index. In the subgroup with a negative index the QRS factor amounted to −0.82 and the T factor to −3.44 on an average. This corresponds to a proportion of 19.2 per cent and 80.8 per cent, respectively. Therefore, in normal individuals the positive index is formed mainly, i.e., in 69.5 per cent, by the QRS factor and the negative index in 80.8 per cent by the T factor. Furthermore, when the observations are classified according to the numerical value of the index into groups 0 to 5, 6 to 10, and over 10 one sees that concomitantly with an increase of the strain index the QRS factor also increases, whereas the T factor decreases. This happens as much in cases of a positive as of a negative index. However, this increase is more marked in the subgroup with a negative index. In the subgroup with a positive index up to +5.0 the QRS factor represented 62.8 per cent of the index, whereas in the group of over +10.0, QRS was 79.6 per cent which equals an increase of 21.1 per cent. In the subgroup with a negative index up to −5.0 the QRS factor averaged 19.3 per cent in the composition of the index; in the group of over −10.0 the latter increased to 68.4 per cent which means an increase of 254.3 per cent.

Correlation of the strain index to Lead I and Lead III: The expression $(R_1 - S_1) - 2T_1$ refers to Lead I whereas $(S_3 - R_3) + 2T_3$ to Lead III. In cases

TABLE I. LEFT VENTRICULAR STRAIN

NO.	AGE (YR.)	STRAIN INDEX	R_1	S_1	T_1	R_3	S_3	T_3	FACTOR		COMPONENT		FORMULA		ANGLE α	CLINICAL DIAGNOSIS
			(MILLIMETERS)						QRS	T	LEAD I	III	WH. AND B.	SCHLOMKA		
1	73	79.5	27.0	0	−6.0	5.5	26.0	+10.0	+47.5	+32.0	39.0	40.5	+47.5	+0.89	−16.0	A.H.D.
2	62	73.0	25.0	0	−6.0	2.0	20.0	+ 9.0	+43.0	+30.0	37.0	36.0	+43.0	+0.95	−15.0	H.H.D.
3	44	68.0	23.0	0	−7.0	0	17.0	+ 7.0	+40.0	+28.0	37.0	31.0	+40.0	+1.00	−15.0	H.H.D.
4	61	65.5	28.0	0	−4.0	4.5	26.0	+ 4.0	+49.5	+16.0	36.0	29.5	+49.5	+0.92	−17.0	H. H.D.
5	46	62.0	19.0	0	−4.5	3.0	25.0	+ 6.0	+41.0	+21.0	28.0	34.0	+41.0	+0.93	−36.0	S.H.D.
6	52	56.0	20.0	0	−3.5	0.5	19.5	+ 5.0	+39.0	+17.0	27.0	29.0	+39.0	+0.98	−28.0	H.H.D.
7	72	54.0	18.0	0	−4.0	2.0	23.0	+ 3.5	+39.0	+15.0	26.0	28.0	+39.0	+0.95	−38.0	A.H.D.
8	51	54.0	14.5	0	−3.5	0.5	23.0	+ 5.5	+37.0	+17.0	20.5	33.5	+37.0	+0.98	−45.0	A.H.D.
9	46	53.0	15.0	0	−3.5	3.0	24.0	+ 5.0	+36.0	+17.0	22.0	31.0	+36.0	+0.93	−46.0	Rh.H.D.
10	36	52.5	22.0	0	−5.5	2.5	18.0	+ 2.0	+37.5	+15.0	33.0	19.5	+37.5	+0.94	−13.0	H.H.D.
11	68	52.5	17.0	0	−4.0	3.5	17.0	+ 8.5	+27.5	+25.0	22.0	30.5	+27.5	+0.81	−18.0	H.H.D.
12	59	51.5	23.0	0	−3.0	0.5	17.0	+ 3.0	+39.5	+12.0	29.0	22.5	+39.5	+0.99	−14.0	H.H.D.
13	58	51.5	17.0	0	−3.5	3.5	22.0	+ 5.0	+34.5	+17.0	24.0	27.5	+34.5	+0.91	−18.0	A.H.D.
14	50	51.5	18.0	0	−2.5	0	19.5	+ 4.5	+37.5	+14.0	23.0	28.5	+37.5	+1.00	−34.0	H.H.D.
15	58	51.5	23.0	0	−3.0	0.5	16.0	+ 3.5	+38.5	+13.0	29.0	22.5	+38.5	+0.99	−12.0	H.H.D.
16	64	51.0	15.0	0	−4.0	2.0	18.0	+ 6.0	+38.0	+13.0	28.0	23.0	+38.0	+0.93	−19.0	H.H.D.
17	53	50.5	15.0	0	−4.0	2.0	18.0	+ 6.0	+31.0	+20.0	23.0	28.0	+31.0	+0.94	−33.0	H.H.D.
18	64	50.5	24.0	0	−3.5	0.5	16.0	+ 2.0	+39.5	+11.0	31.0	19.5	+39.5	+0.99	−10.0	H.H.D.
19	51	50.0	12.0	0	−3.0	6.0	24.0	+ 7.0	+30.0	+20.0	18.0	32.0	+30.0	+0.83	−44.0	A.H.D.
20	54	50.0	21.0	0	−4.5	2.0	18.0	+ 2.0	+37.0	+13.0	30.0	20.0	+37.0	+0.95	−16.0	H.H.D.
21	78	49.5	15.5	0	−4.0	2.0	19.0	+ 4.5	+32.5	+17.0	23.5	26.0	+32.5	+0.94	−35.0	H.H.D.
22	69	48.5	18.0	0	−3.0	0.5	19.0	+ 3.0	+36.5	+12.0	24.0	24.5	+36.5	+0.98	−32.0	S.H.D.
23	52	48.0	20.5	0	−2.0	0.5	21.0	+ 1.5	+41.0	+ 7.0	24.5	23.5	+41.0	+0.99	−30.0	H.H.D.
24	60	47.0	14.0	0	−2.5	3.0	19.0	+ 6.0	+30.0	+17.0	19.0	28.0	+30.0	+0.91	−37.0	H.H.D.
25	73	47.0	20.0	0	−1.5	1.0	19.0	+ 3.0	+38.0	+ 9.0	23.0	24.0	+38.0	+0.95	−24.0	A.H.D.
26	52	46.5	16.0	0	−3.0	0	16.5	+ 4.0	+32.5	+14.0	22.0	24.5	+32.5	+1.00	−28.0	H.H.D.
27	58	46.0	18.0	0	−3.0	1.0	17.0	+ 3.0	+34.0	+12.0	24.0	22.0	+34.0	+0.97	−23.0	H.H.D.
28	44	44.0	18.5	0	−4.0	2.5	13.0	+ 3.5	+29.0	+15.0	26.5	17.5	+29.0	+0.92	−18.0	Rh.H.D.
29	65	43.5	21.0	0	−2.5	0.5	14.0	+ 2.0	+34.5	+ 9.0	26.0	17.5	+34.5	+0.99	− 9.0	H.H.D.
30	68	43.0	19.0	0	−2.5	0	15.0	+ 2.0	+34.0	+ 9.0	24.0	19.0	+34.0	+1.00	−13.0	H.H.D.

Key: H.H.D., Hypertensive heart disease; A.H.D., Arteriosclerotic heart disease; S.H.D., Syphilitic heart disease; Rh.H.D., Rheumatic heart disease.

with a positive index, Lead I contributes 57 per cent, and Lead III 43 per cent in determining the numerical value of the strain index. In cases with a negative index the values vary significantly. Lead I represents only 6.9 per cent and Lead III 93.1 per cent of the index.

Correlation between the strain index and the position of the electrical axis: Observations were classified into groups 0 to 5.0, 6.0 to 10.0, and over 10.0, both positive and negative according to the strain index. The corresponding average values of the White and Bock formula, of the Schlomka formula, and of the angle α were determined in each group. A parallelism, though not in a mathematical sense, was found between the increase of the strain index and a shift of the electrical axis to the left as expressed by these formulae. By comparing average values in the subgroup with a positive index at the lowest degree of the strain index from 0 to +5.0 with that over +10.0, there was an increase of the strain index of 366 per cent, the increase of the White and Bock formula was 160 per cent; Schlomka showed 48 per cent; and the angle α 114 per cent of left-axis deviation. The same comparison in the subgroup with a negative index showed an average increase of the strain index of 387 per cent, practically identical with that found in the subgroup with a positive index which was 366 per cent. The White and Bock formula presented an average increase of 471 per cent, and the Schlomka index revealed the greatest increase averaging 563 per cent. The angle α was less sensitive as the average increase was only 45 per cent.

The strain index showed a more intimate correlation with the formula of White and Bock, with the pecularity that its positive average values were less and its negative values were greater.

Left Ventricular Strain (Table I).—Among fifty records presenting in a very clear form the electrocardiographic patterns of left ventricular strain, thirty-seven were those of patients with hypertensive heart disease, nine with valvular lesions, and four with arteriosclerotic heart disease. Their age averaged 58 years, with a range from 44 to 78.

Strain index: It was always positive, with an average value of +47.2 with a maximum of +79.5 and a minimum of +32.5. Distribution of index values was from 31 to 40, fourteen cases; 41 to 50, eighteen cases; 51 to 60, thirteen cases; 61 to 70, three cases; and over 70, two cases.

Correlation of the strain index with the QRS and T factors: The direction of the T wave was always opposite to the main deflection of the ventricular complex as much in Lead I as in Lead III. Composition of the average left ventricular strain index +47.2 consisted in 33.4 QRS factor (71.6 per cent) and 13.8 as T factor (28.4 per cent). Increase of the strain index occurs mainly by increase of the T factor. In the lowest group of strain index with an average value +37.0 the QRS factor amounted to 74.3 per cent and the T factor to 25.7 per cent. In the highest group the strain index averaged +76.2, the QRS factor represented 59.3 per cent, and the T factor 40.7 per cent of the index. It can be seen that changes of T waves become increasingly important with an increasing ventricular strain.

Correlation of the strain index with Leads I and III: Leads I and III contribute almost in equal proportion in the numerical determination of the index.

TABLE II. RIGHT VENTRICULAR STRAIN

NO.	AGE (YR.)	STRAIN INDEX	R_1	S_1	T_1	R_2	S_2	T_2	FACTOR		COMPONENT		FORMULA		ANGLE α	CLINICAL DIAGNOSIS
			(MILLIMETERS)						QRS	T	LEAD I	III	WH. AND B.	SCHLOMKA		
1	38	−40.0	8.0	13.0	+1.5	22.0	0	−5.0	−27.0	−13.0	− 8.0	−32.0	−27.0	−0.77	106.0	Cong.H.D.
2	35	−38.5	2.5	7.0	+1.0	29.0	5.0	−4.0	−28.5	−10.0	− 6.5	−32.0	−28.5	−0.79	100.0	Cong.H.D.
3	30	−38.0	5.0	7.0	+0.5	27.0	0	−4.0	−29.0	− 9.0	− 3.0	−35.0	−29.0	−0.83	94.0	Cong.H.D.
4	13	−38.0	3.0	11.0	+5.0	16.0	0	−2.0	−24.0	−14.0	−18.0	−20.0	−24.0	−0.88	120.0	Cong.H.D.
5	18	−34.0	2.0	13.0	+3.0	15.0	2.0	−2.0	−24.0	−10.0	−17.0	−17.0	−24.0	−0.86	141.0	Cong.H.D.
6	25	−33.5	3.0	10.5	+1.0	16.0	0	−4.0	−23.5	−10.0	− 9.5	−24.0	−23.5	−0.85	119.0	Cong.H.D.
7	45	−32.5	6.0	13.0	+1.5	17.5	0	−2.5	−24.5	− 8.0	−10.0	−22.5	−24.5	−0.83	113.0	Cong.H.D.
8	30	−32.0	5.0	7.0	+0.5	22.0	0	−3.5	−24.0	− 8.0	− 3.0	−29.0	−22.0	−0.95	140.0	Mitr.sten.
9	26	−32.0	1.0	11.0	+2.5	12.0	0	−2.5	−22.0	−10.0	−15.0	−17.0	−26.0	−0.87	108.0	Mitr.sten.
10	38	−31.0	4.0	10.0	+1.0	20.0	0	−1.5	−26.0	− 5.0	− 8.0	−23.0	−19.0	−0.95	122.0	Rh.H.D.
11	10	−29.0	1.0	8.0	+3.0	12.0	0	−2.0	−19.0	−10.0	−13.0	−16.0	−19.0	−0.87	90.0	Mitr.sten.
12	49	−29.0	3.0	3.0	+2.5	19.0	0	−2.5	−19.0	−10.0	− 5.0	−24.0	−17.0	−0.85	124.0	Cor pulm.
13	60	−27.0	3.0	9.0	+1.0	11.0	0	−4.0	−17.0	−10.0	− 8.0	−19.0	−19.5	−0.88	140.0	Cor pulm.
14	57	−25.5	2.5	11.0	+2.0	11.0	0	−1.0	−19.5	− 6.0	−12.5	−13.0	−19.5	−0.87	136.0	Cong.H.D.
15	14	−25.5	1.5	3.0	+1.5	14.0	0	−4.0	−16.5	− 9.0	− 4.5	−21.0	−18.5	−0.85	98.0	Bronch.asth.
16	43	−25.5	3.0	5.5	+0.5	14.0	0	−4.0	−16.5	− 9.0	− 3.5	−22.0	−16.5	−0.84	101.0	Mitr.sten.
17	43	−25.5	3.5	4.0	+2.0	15.0	0	−3.0	−15.5	−10.0	− 4.5	−21.0	−15.5	−0.81	99.0	Mitr.sten.
18	49	−25.5	2.0	1.5	+1.0	18.0	0	−3.0	−17.5	− 8.0	− 1.5	−24.0	−17.5	−0.95	89.0	Mitr.sten.
19	43	−25.0	2.5	5.0	+1.0	13.5	0	−3.5	−16.0	− 9.0	− 4.5	−20.5	−16.0	−0.86	100.0	Cong.H.D.
20	21	−24.0	1.0	4.0	+1.5	14.0	1.0	−2.5	−16.0	− 8.0	− 6.0	−18.0	−16.0	−0.88	105.0	Mitr.sten.
21	21	−24.0	1.0	3.0	+2.0	12.0	0	−3.0	−14.0	−10.0	− 6.0	−18.0	−14.0	−0.93	100.0	Mitr.sten.
22	10	−23.0	0.5	6.5	+2.5	8.0	0	−2.0	−14.0	− 9.0	−11.0	−12.0	−14.0	−0.96	132.0	Rh.H.D.
23	49	−23.0	1.5	1.5	+2.5	15.0	0	−1.5	−15.0	− 8.0	− 5.0	−18.0	−15.0	−0.91	90.0	Mitr.sten.
24	10	−22.5	1.0	7.0	+2.0	8.5	0	−2.0	−14.5	− 8.0	−10.0	−12.5	−14.5	−0.94	132.0	Rh.H.D.
25	43	−22.0	3.0	2.0	+0.5	15.0	0	−3.0	−15.0	− 7.0	0	−22.0	−15.0	−0.83	88.0	Rh.H.D.
26	10	−21.5	4.5	6.0	+3.0	18.0	0	−2.0	−19.5	− 2.0	− 7.5	−14.0	−19.5	−0.81	96.0	Mitr.sten.
27	43	−21.5	3.5	5.0	+0.5	13.0	0	−2.0	−14.5	− 7.0	− 2.5	−19.0	−14.5	−0.80	96.0	Rh.H.D.
28	26	−21.0	4.0	9.0	+2.0	10.0	0	−1.0	−15.0	− 6.0	− 9.0	−12.0	−15.0	−0.78	122.0	Rh.H.D.
29	24	−21.0	2.5	4.5	+2.0	11.0	0	−2.0	−13.0	− 8.0	− 6.0	−15.0	−13.5	−0.84	101.0	Rh.H.D.
30	29	−20.0	2.0	0	+2.0	15.0	0	−1.5	−13.0	− 7.0	− 2.0	−18.0	−13.0	−0.80	85.0	Rh.H.D.

Lead I represents on an average 51.8 per cent, and Lead III 48.2 per cent of the left ventricular strain index.

Strain index and position of the electrical axis: Changes of the strain index with different positions of the electrical axis were less pronounced and showed lack of parallelism as compared with normal individuals. When comparing the corresponding average values in the lowest and highest group of the strain index the increase of the left ventricular strain index was 106 per cent; the White and Bock formula showed an increase of 60 per cent with a parallelism throughout the whole extension of the strain index. The Schlomka index showed no changes, and there was no parallelism whatsoever with the strain index. Its average values remained without variations at different levels of the strain index. At the lowest and highest values of the strain index the angle α remained practically equal being $-14.5°$ and $-15.5°$, respectively, whereas from 41 to 50 showed an average value of $-27.3°$; from 51 to 60, $-25.2°$; and from 61 to 70, $-23.0°$. Thus the increase of the numerical value of the strain index was not followed by identical changes of the angle α.

Clinical correlations of the strain index in cases of left ventricular strain: The strain index bears no relation to the clinical diagnosis or to etiologic factors. It measures in a nonspecific way the degree of overactivity of the ventricular musculature caused by whatever conditions.

Right Ventricular Strain (Table II).—The thirty observations of this group were mostly cardiac patients with valvular lesions: eighteen with mitral stenosis, one with a combined mitral and aortic lesion, one with pulmonary stenosis, seven with congenital heart disease, two with chronic cor pulmonale, and one with bronchial asthma. Their age averaged 31.3 years, with a range from 10 to 60.

Strain index: It was always negative with an average value of -27.6 and with a range from -20.0 to -40.0. Distribution of the index according to its numerical value was as follows: from -21.0 to -30.0, twenty cases; from -31.0 to -40.0, ten cases.

Correlation of the strain index with the QRS and T factors: The QRS factor averaged -19.7 which represents 68.8 per cent of the average right ventricular strain index; the average T factor was -8.5, i.e., 31.2 per cent, a similar situation to that which was found in the group of left ventricular strain. An increase of the right ventricular strain index is due mostly to an increase of the QRS factor, contrary to what takes place in cases of left ventricular strain. In the group of the lowest average strain index the QRS factor was 67.1 per cent, and the T factor, 32.9 per cent. At the highest level of the right ventricular strain index the QRS factor amounted to 72.3 per cent and the T factor to 27.7 per cent.

Correlation of the strain index to Leads I and III: The contribution of the two standard leads in the numerical determination of the strain index was unequal. Lead I represented 26.5 per cent, and Lead III, 73.5 per cent of the average strain index.

Strain index and position of the electrical axis: The right ventricular strain index and the White and Bock formula showed an identical behavior. An average increase of 45 per cent of the strain index was accompanied by an average increase of 56 per cent of the White and Bock formula. On the contrary, the Schlomka index showed practically no changes with the increase of the strain index. Its average value of -0.867 decreased to -0.846 (-3.0 per cent) when the strain index increased 56 per cent. The angle α increased its numerical value with increasing negativity of the strain index, but its changes were limited, being only 7 per cent.

DISCUSSION

Strain in the ventricular musculature develops when working requirements are beyond the functional capacity of the affected ventricle. A state of exhaustion is the result, and characteristic changes in the electrocardiogram, the so-called strain pattern, are produced. The latter consists in an axis deviation, an inversion of the T waves and deviations of the RS-T segment. Besides these well-known features in the extremity leads there exist important signs in the precordial leads as established by Sokolow and Lyon and confirmed by Myers and associates,[6] Gordon and Goldberg,[7] and other authorities. The exact mechanism responsible for the electrocardiographic strain pattern is still not well understood; changes in the metabolism of the ventricular musculature such as an increased hydrogen ion concentration as suggested by Barnes and Whitten,[1] loss of potassium in the strained muscle (Goldberger),[8] cardiac anoxia on the one hand, and circulatory disturbances as coronary insufficiency on the other hand, have been invoked by different authors. Scherf and Boyd[9] attribute predominant importance to disturbances of the intraventricular spread of activation.

Diagnosis and appreciation of the severity of ventricular strain are based on the presence of various qualitative, descriptive criteria and quantitative measured data as much in the standard leads as in the precordial and extremity leads. In the present paper a new empirical formula is given that combines in a single expression changes of the QRS complex and T wave in the first and third limb leads. This formula demonstrates a satisfactory parallelism with the intensity of ventricular strain. This strain index is composed of the QRS factor whose increase is related mainly but not exclusively to the overactivity of the strained ventricular musculature and of the T factor, whose changes in direction as in voltage are related to the myocardial involvement due to sustained strain. Excessive work causes hyperactivity and later on hypertrophy both leading to an increase of the voltage of the QRS complex and finally to a lowering or inversion of the T wave as an ultimate consequence.

These changes are different in direction but convergent in sense, and they appear in cases of left ventricular strain first in Lead I and are followed by similar changes in Lead III. On the contrary, in cases of right ventricular strain they begin in Lead III and are followed later by changes in Lead I. Since the height of the T wave, especially in cases of ventricular strain, represents only a part of the height of the QRS complex, it was found necessary to increase the numerical

importance of the changes of the T wave by multiplying with a factor that by experience proved to be 2. Thus the formula of the strain index

$$[(R_1 - S_1) - 2T_1] + [(S_3 - R_3) + 2T_3]$$

transforms the divergence of changes of the QRS and T factors into an accordant sense by mathematical coordination and adjusts the importance of the T factor by multiplying with an empirical factor. Finally, separate changes of Leads I and III, which have identical sense and importance, combine by addition.

It was found that the QRS factor of the strain index numerically was always identical with the values derived from the formula of White and Bock. The expressions of (R_1-S_1) and (S_3-R_3) that figure in our formula and which were conceived with the specific purpose of reducing both waves in the same lead in a single lineal measure, in spite of its different structure, coincide exactly with the formula of White and Bock, as can be demonstrated mathematically:

$$(R_1 + S_3) - (R_3 + S_1) = R_1 + S_3 - R_3 - S_1 = (R_1 - S_1) + (S_3 - R_3)$$

which is a component of the strain index.

With the purpose of establishing basic facts the strain index was studied in 100 healthy individuals, where ventricular strain does not exist. The strain index was positive in sixty-four and negative in thirty-six instances. Its mean value was found to be $+1.84$, with a standard deviation of ± 5.58 and with equal range in both directions of ± 12.5. There was a definite tendency toward negative values in the younger group up to 30 years, and toward positive values over this age, a situation which is doubtless related to the orientation of the electrical position of the heart at different ages. All methods that measure the position of the electrical axis agree that in younger individuals the vertical position prevails, and consequently with a right-axis deviation. On the contrary, with increasing age a tendency toward a horizontal position exists that causes a shift of the electrical axis to the left. As to the composition and relative proportion of the QRS and T factors, the T factor must always be substracted from the QRS factor, because T_1 in healthy subjects is always positive, and our formula, due to its structure, transforms its positivity into a negative value. The average strain index in the positive subgroup was $+5.07$ and -4.26 in the negative subgroup. Extreme values over ± 10.0 were observed in three instances only.

In cases of left ventricular strain the situation was entirely different. The strain index was always positive. Its maximum value of $+79.5$ was observed in a case of manifest left ventricular strain, and its minimum value of $+32.5$ in cases where signs of ventricular strain were only slight. Therefore, the strain index separates normal records from those of cases with left ventricular strain in a clear manner. The lowest observed strain index of $+32.5$ was distant from normal records whose average index measured $+1.84$ only, and distant even from the highest value of $+12.5$ observed only exceptionally (Fig. 1).

Between the boundaries of the normal zone and the left ventricular strain the intermediate zone is located. Near to the normal limit are those records that

exhibit marked positional changes with or without associated hypertrophy, and initial changes of left ventricular hypertrophy. Near to the lower limit of the left ventricular strain are those cases with initial stages of ventricular strain and also advanced stages of left ventricular strain in which there is a marked myocardial damage. Because of this circumstance a decrease of voltage both of QRS and T waves takes place, as can be seen frequently, e.g., in cases of decompensated hypertension.

The strain index in cases of right ventricular strain was always negative; its average value was −27.6, with a range from −20.0 to −40.0. In these cases the intermediate zone was more reduced. The lower limit of manifest cases of right ventricular strain is nearer to the upper limit of normal records. Considerations concerning electrocardiograms of the left intermediate zone are valid also for the right intermediate zone.

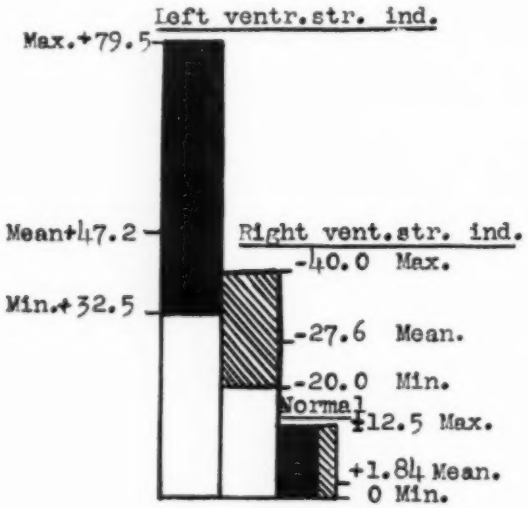

Fig. 1.—Comparative values of the strain index (maximum, minimum, and mean) in cases of left and right ventricular strain and in normal condition.

The behavior of the QRS and T factors in cases of left and right ventricular strain was different from that in normal records. The direction of T wave was always contrary to that of the main deflection of the QRS complex, whether there existed left or right ventricular strain. Therefore, the T factor contributed to increase, by summation with the value of the QRS factor. This mechanism explains the high value of the index in cases of ventricular strain.

The participation of the QRS and T factors in the formation of the left and right ventricular strain index is very similar. In cases of left ventricular strain the QRS factor contributes with 71.6 per cent and the T factor with 28.4 per cent. In cases of right ventricular strain the proportion is 68.8 per cent and 31.2 per cent, respectively. However, there exists a difference between both with respect to the mechanism by which the increase of the strain index is operated. Increase

of the left ventricular strain index is determined mainly by an increase of the T factor, whereas the right ventricular strain index increases are mainly due to an increase of its QRS factor.

Leads I and III partake in a different proportion in determining the value of the index in cases of left or right ventricular strain. The left ventricular strain index is formed almost in equal proportion by Leads I and III, with 51.8 per cent and 48.2 per cent, respectively. In contrast, Lead I represents only 26.5 per cent of the right ventricular strain index, whereas Lead III contributes predominantly with 73.5 per cent.

The sum of voltages R_1+S_3 which according to Gubner and Ungerleider[10] indicates the presence of left ventricular hypertrophy, if it is greater than 25, was in every case fulfilled in the group of left ventricular strain, its average value being 35.39, with a range from 26.0 to 54.0.

The study of a possible correlation between strain index and different methods of determination of the electrical axis has given poor results. In normal individuals there exists a parallelism between changes of the strain index and the corresponding values of White and Bock, of the Schlomka formulas, and of the angle α. Increase of the positive values of the strain index was accompanied by a deviation of the position of the electrical axis to the left; inversely, in cases of an increased negative strain index right-axis deviation was observed. In cases of left or right ventricular strain a correlation was found only between the strain index and the White and Bock formula, whereas a correlation was absent with respect to Schlomka's formula and the angle α. On the other hand, determination of the electrical axis as a measure of ventricular hypertrophy has been proved less successful. It is now clear that rotation and cardiac position are more important in the determination of the extremity potentials and thus of the position of the electrical axis than chamber hypertrophy alone (Kroop and associates).[11] Decisive for the form of the electrocardiogram is the relative position of the cardiac chambers to the extremities, and this depends essentially on body build and only secondarily on cardiac conditions. Therefore, real left ventricular hypertrophy in vertically located hearts may produce right-axis deviation and vice versa (Goldberger,[8] Kossmann[12]). Furthermore, individual differences in the arrangement of the ventricular conductive system or eventual disturbances in the interventricular conduction are other complicating circumstances that may alter the aspect of the ventricular complex and so also the position of the electrical axis. Consequently, the position of the electrical axis and ventricular hypertrophy are not simple coordinate concepts although they usually coexist; however, exceptions are frequent. The strain index is a measure of the condition of the ventricular musculature, whereas the various formulas and angle α deal with the position of the electrical axis. Both expressions may or may not be concomitant because they are different as much in their mechanism as in their significance.

In clinical application the strain index indicates merely the degree of participation of the ventricular musculature without relation to diagnosis. A positive or negative index of less than 12.5 indicates normality. A positive strain index

greater than 12.5 but less than 32.5 is suggestive of positional changes and of marked hypertrophy of the left ventricle. Left ventricular strain is present in increasing severity in cases of a positive index of an even higher value. The maximum strain index observed in the present study was of 79.5. A negative strain index indicates right ventricular strain whose manifest lowest value was found −20.0.

The correct evaluation of the strain index requires not only a detailed electrocardiographic analysis but also complete knowledge of the clinical condition of the patient. Indeed, whether pure positional changes, hypertrophy, single or combined, or ventricular strain are present cannot be determined exactly on the basis of the numerical value of the strain index alone; however, extreme values are in themselves of definite significance.

SUMMARY

1. A new index for the quantitative estimation of ventricular strain is described. This index combines in a single expression the two most constant quantitative changes of ventricular strain pattern, i.e., those of the QRS complex and T wave in the following form:

$$[(R_1 - S_1) - 2T_1] + [(S_3 - R_3) + 2T_3] \quad .$$

2. Standard values are established in a group of 100 healthy individuals. The mean was found to be +1.84 with a range from −12.5 to +12.5. In cases of left ventricular strain the index is always positive, with a mean of +47.2 and a range from +32.5 to +79.5. In cases of right ventricular strain the index is always negative with a mean of −27.6 and a range from −20.0 to −40.0.

3. Correlations between the strain index and its components the QRS and T factors, Leads I and III, and the position of the electrical axis are established as much in normal individuals as in cases of left and right ventricular strain. Their pathophysiologic and clinical aspects are discussed.

4. The strain index expresses in a quantitative manner the intensity of the response of the ventricular musculature to the required overwork, regardless of causative factors. It serves to indicate by a quantitative criterion the presence of ventricular overactivity and permits following and comparing the mentioned changes in different cardiac conditions.

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A MATHEMATICAL METHOD TO DETERMINE THE MAGNITUDE OF ELECTRICAL AXIS

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IN A foregoing communication,[1] a method to determine the direction of electrical axis was proposed. To complete the determination of this electrical axis it is necessary to find its magnitude.

This magnitude may be calculated either by standard limb leads or by unipolar limb leads. Three formulas were proposed by Einthoven[2]:

1. $E = e_1/\cos X$
2. $E = e_2/\cos (60-X)$
3. $E = e_3/\cos (120-X)$

If one wants to determine electrical-axis magnitude with the help of Wilson's and Goldberger's leads, one must remember standard leads are augmented 1.7322 in relation to Wilson's leads[3] and 1.1548 in relation with Goldberger's leads.

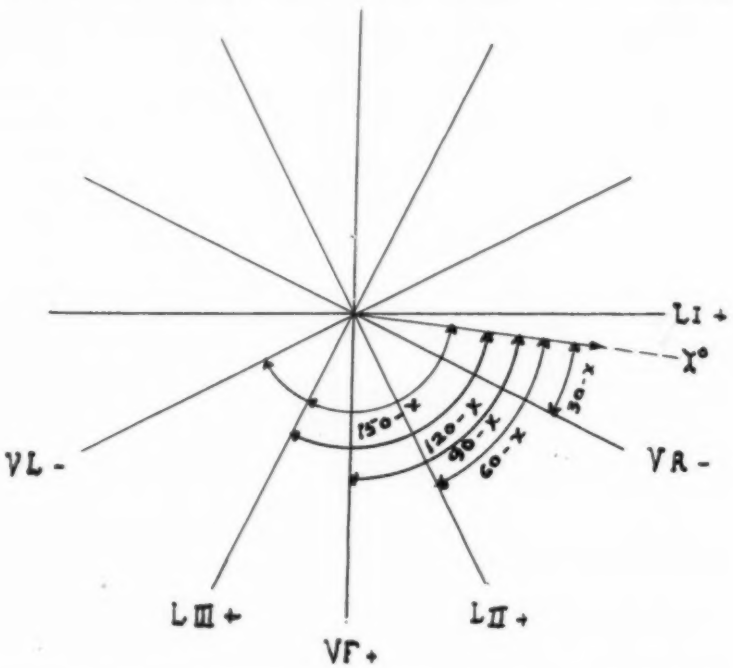

Fig. 1.—Illustrating the relation between the limb leads and angle *X* or electrical-axis direction. It is self-demonstrative of the proposed formulas.

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TABLE I. OBTAINED WITH LIMB LEADS (IN THE LEFT COLUMN) AND WITH POSSIBLE DIRECTION OF ELECTRICAL AXIS EXPRESSED BY ANGLES (IN THE TOP AND LAST LINE)

LIMB LEADS	ANGLE X																	
	0°	+10°	+20°	+30°	+40°	+50°	+60°	+70°	+80°	+90°	+100°	+110°	+120°	+130°	+140°	+150°	+160°	+170°
L I	1.000	1.015	1.064	1.155	1.305	1.556	2.000	2.924	5.760	?	5.760	2.924	2.000	1.556	1.305	1.155	1.064	1.015
L II	2.000	1.556	1.305	1.155	1.064	1.015	1.000	1.015	1.064	1.155	1.305	1.556	2.000	2.924	5.760	?	5.760	2.924
L III	2.000	2.924	5.760	?	5.760	2.924	2.000	1.556	1.305	1.155	1.064	1.015	1.000	1.015	1.064	1.155	1.305	1.556
VR	2.000	1.843	1.759	1.732	1.759	1.843	2.000	2.261	2.695	3.464	5.065	9.978	?	9.978	5.065	3.464	2.695	2.261
VL	2.000	2.261	2.695	3.464	5.065	9.978	?	9.978	5.065	3.464	2.695	2.261	2.000	1.843	1.759	1.732	1.759	1.843
VF	?	9.978	5.065	3.464	2.695	2.261	2.000	1.843	1.759	1.732	1.759	1.843	2.000	2.261	2.695	3.464	5.065	9.978
aVR	1.333	1.229	1.173	1.155	1.173	1.229	1.333	1.507	1.796	2.310	3.377	6.652	?	6.652	3.377	2.310	1.796	1.507
aVL	1.333	1.507	1.796	2.310	3.377	6.652	?	6.652	3.377	2.310	1.796	1.507	1.333	1.229	1.173	1.155	1.173	1.229
aVF	?	6.652	3.377	2.310	1.796	1.507	1.333	1.229	1.173	1.155	1.173	1.229	1.333	1.507	1.796	2.310	3.377	6.652
	±180°	−170°	−160°	−150°	−140°	−130°	−120°	−110°	−100°	−90°	−80°	−70°	−60°	−50°	−40°	−30°	−20°	−10°

These aforementioned leads must be corrected, and then the same results may be obtained for the same electrocardiogram.

By keeping in mind these mathematical relations, the following formulas are here proposed:

4. $E = 1.7322\ e_{VR}/\cos\ (30-X)$
5. $E = 1.7322\ e_{VL}/\cos\ (150-X)$
6. $E = 1.7322\ e_{VF}/\cos\ (90-X)$
7. $E = 1.1548\ e_{aVR}/\cos\ (30-X)$
8. $E = 1.1548\ e_{aVL}/\cos\ (150-X)$
9. $E = 1.1548\ e_{aVF}/\cos\ (90-X)$

In these formulas, E represents the magnitude of the resulting vector; e_1, e_2, ... e_{aVF} represent the projection of that vector upon lines representing all extremity leads, and *X* represents the angle which indicates the direction of the vector.

Mathematical demonstration for these proposed formulas is not necessary and they may be obtained by simply following Fig. 1.

To facilitate the obtention of the magnitude of electrical axis, Table I is presented. The table was obtained by means of application of formulas. The results are expressed in units similar to those chosen to measure limb leads. The sign of limb leads has been disregarded, because the results are absolute values. The number found in the table must be multiplied by the value found for each lead, because the table was calculated with a theoretical value of 1 for the limb leads.

SUMMARY AND CONCLUSIONS

An exact method to calculate electrical-axis magnitude is presented, with the help of the three formulas presented previously by Einthoven and six other formulas proposed here.

A table to facilitate the procedure is presented for the theoretical application of these formulas.

The proposed method is applicable to all electrocardiographic waves or complexes.

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THORACIC BALLISTOCARDIOGRAPHY

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THE standard ballistocardiogram primarily reflects the oscillation of the body mass in response to two major forces: ventricular ejection and the subsequent movement of blood in the aorta.[1-3] These major oscillations occur in a narrow-frequency range close to the natural resonant frequency of the body.[1] Other important cardiac forces which produce oscillations outside of this frequency range are so attenuated as to have only minor representation in the tracing.

A record which would reflect more specifically all the important cardiac forces should be of value in estimating heart function. Two body areas may be utilized to study more selectively the ballistic effects of these cardiac forces. First, some of the damping by extracardiac tissues may be diminished by recording from a local body surface area close to the heart, for example, the interscapular area. Second, cardiac action may be partially divorced from aortic and main body mass oscillation by recording from the sternal region, an area which is not only close to the heart and distant from the main portion of the aorta, but also one which may be moved independently of the main body mass by virtue of the hinging action of the ribs.

METHOD

Records have been obtained with a 6 by 6 inch transducer[4] whose flat springs have been replaced by coil springs. This transducer has been found to give the same response as the uniaxial flat-spring platform transducer. In order to record simultaneous longitudinal and lateral ballistocardiographic tracings, two magnet-coil systems with capacitance filters of 20 microfarads have been used to record motion along the two axes. Records from this apparatus have not been standardized, because concern has been directed toward qualitative rather than quantitative phenomena.

Interscapular records have been obtained by placing the subject in the supine position on a rigid table whose top has an opening through which the transducer platform is applied directly to the body. The subject is so located that the spine of C-7 is aligned with the headward edge of the platform. Sternal records have been obtained in the same manner with the subject in the prone

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position and the body so located that the sternal angle is aligned with the headward edge of the platform.

The interscapular ballistocardiograms have been recorded with simultaneous tracings of the heart sounds, Lead I of the electrocardiogram, respirations, and the standard Dock ballistocardiograph on the legs. Sternal ballistocardiograms were recorded with simultaneous tracings of Lead I of the electrocardiogram, respiration, and, in some cases, heart sounds.

Tracings have been obtained from fifty-eight normal subjects: thirty-nine males and nineteen females, ranging from 13 to 53 years of age.

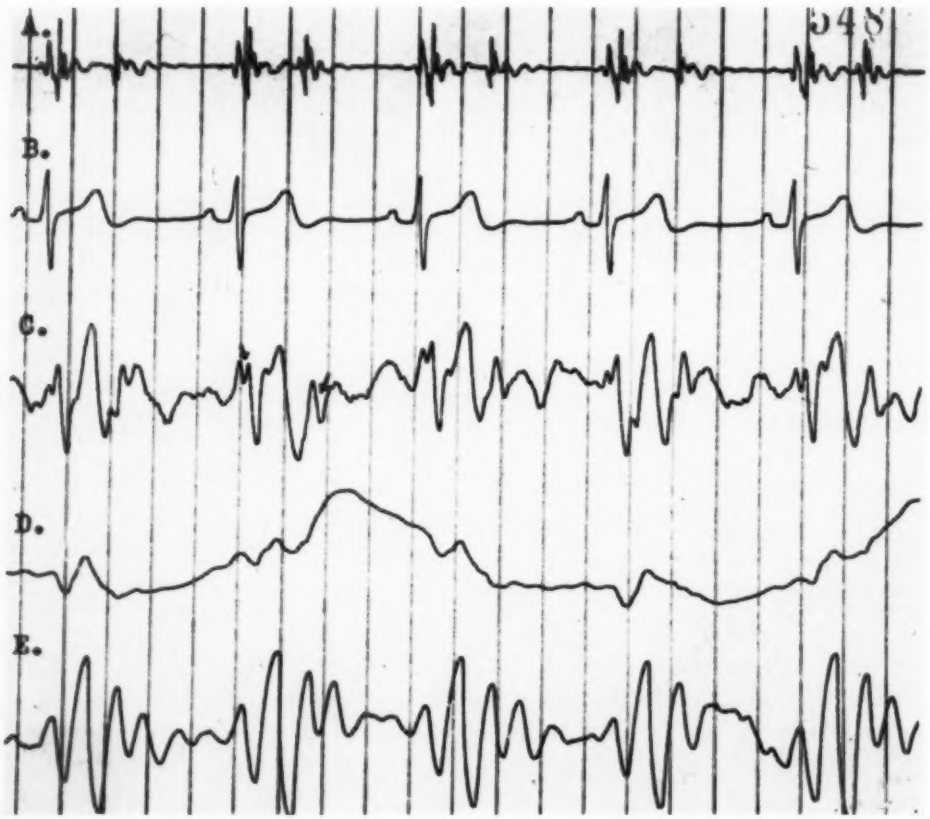

Fig. 1.—Longitudinal interscapular ballistocardiogram. Simultaneous tracings. *A*, Heart sounds from the apex. *B*, Lead I of the electrocardiogram. *C*, Longitudinal interscapular ballistocardiogram. Arrows on the H and L waves indicate the higher frequency oscillations in time with the heart sounds. The J wave is bi-peaked and shows respiratory variation of the peaks. *D*, Respiration. Inspiration is up. *E*, Standard ballistocardiogram from the legs.

RESULTS

The longitudinal interscapular ballistocardiogram is similar to tracings recording total body longitudinal motion. The H wave, however, is changed by higher* frequency oscillations synchronous with isometric contraction of the

*Higher than 10 cycles per second.

ventricles and the first heart sound (Fig. 1). Close to the L peak there is noted in some tracings, a second series of higher frequency oscillations synchronous with the second heart sound. These two groups of higher frequency oscillations have been related to the closing of the heart valves.[4]

The peak of the J wave tends to be blunted and occasionally shows a double peak. The first peak increases in amplitude during inspiration and the second peak increases during expiration.

The lateral interscapular tracing has a more variable pattern (Fig. 2). In 90 per cent of the cases the lateral tracing is similar to the longitudinal interscapular tracing except that the complexes are not exactly synchronous with the longitudinal waves. Of this group about one-half the waves which occur at the approximate time of the standard J wave are directed toward the left, and the

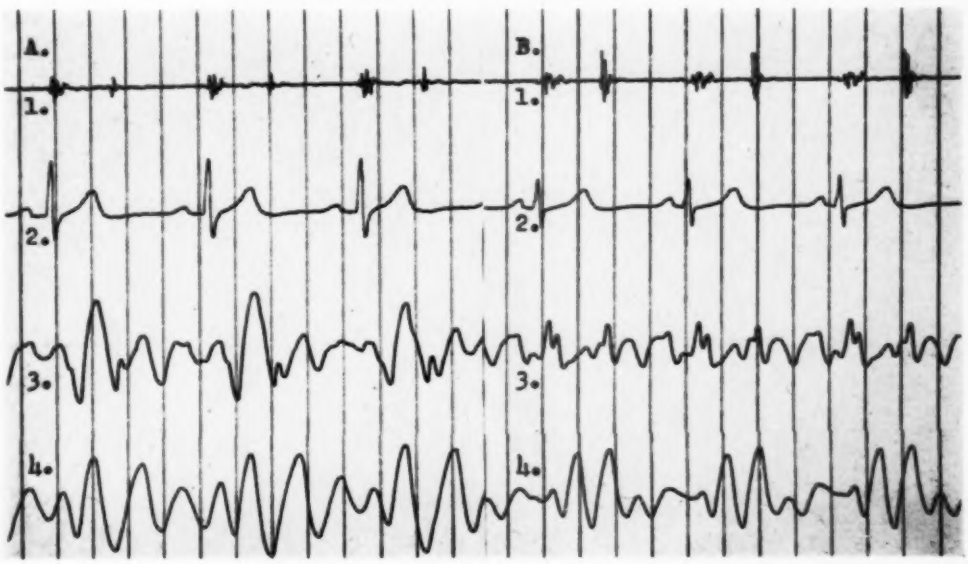

Fig. 2.—Lateral interscapular ballistocardiogram. *A*, Simultaneous tracings. *1*, Heart sounds from the apex. *2*, Lead I of the electrocardiogram. *3*, Lateral interscapular ballistocardiogram. The dominant wave in time with the J wave of the standard tracing from the legs, *4*, is directed toward the right. *B*, Simultaneous tracings. *1*, Heart sounds from the apex. *2*, Lead I of the electrocardiogram. *3*, Lateral interscapular ballistocardiogram with a minor rightward (upward) wave in approximate time with the J wave in the standard tracing from the legs, *4*.

other one-half are directed toward the right. This variation is similar to that described by Brandt and associates.[5] The tracing in the remaining 10 per cent of the whole group shows a low amplitude wave at the time of the J wave in the longitudinal tracing, and frequently larger low frequency diastolic waves. Bipeaking of the J wave is noted in some of these tracings.

The longitudinal sternal ballistocardiogram shows two main patterns, one of which appears to reflect primarily cardiac activity (Fig. 3). In this cardiac form there is a sharp headward stroke which begins shortly after the beginning of the QRS complex. Close to the peak of this stroke there are small higher frequency oscillations which are synchronous with the first heart sound. These oscillations are followed by a sharp footward stroke which rounds out into a large

rising curve. This curve is interrupted by a second series of small higher frequency oscillations which are synchronous with the second heart sound. Following these oscillations, the large low-frequency wave continues as a headward stroke, which rounds out and continues footward to the beginning of the next cycle. Just preceding the first systolic headward stroke there is a short irregular footward stroke which begins at or shortly after the peak of the P wave.

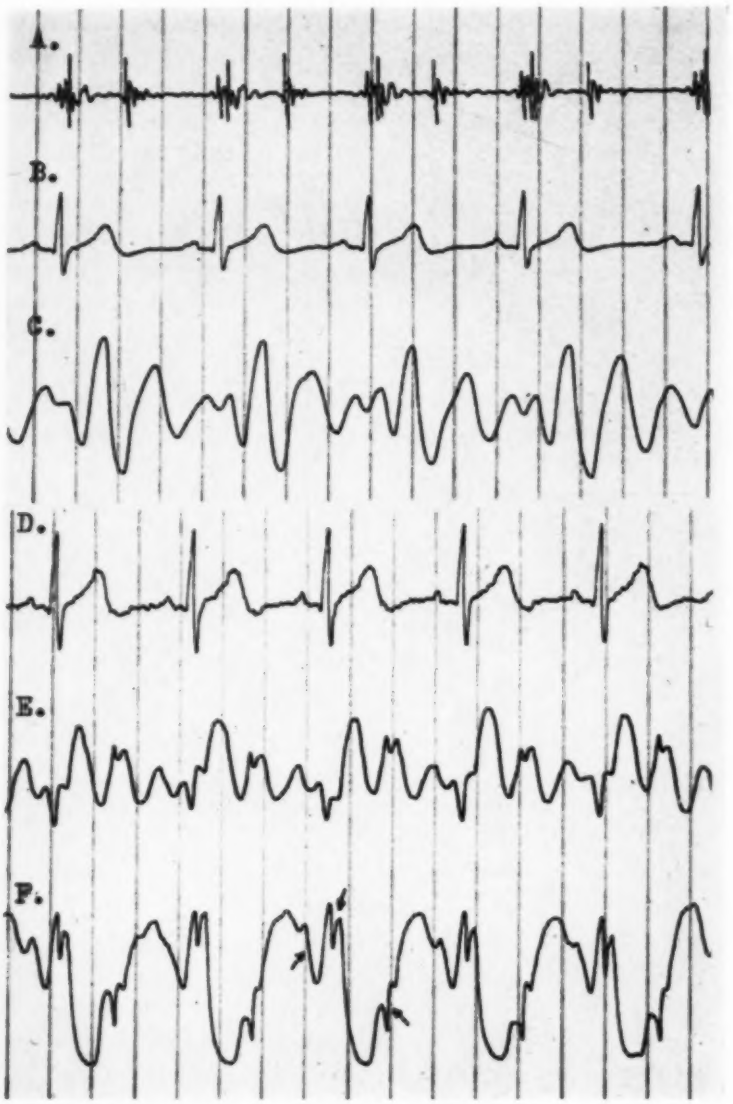

Fig. 3.—Longitudinal and lateral sternal ballistocardiograms. Simultaneous supine tracings. *A*, Heart sounds from the apex. *B*, Lead I of the electrocardiogram. *C*, Standard ballistocardiogram from the legs. Simultaneous prone tracings on the same subject. *D*, Lead I of the electrocardiogram. *E*, Lateral sternal ballistocardiogram. Leftward motion is upward. *F*, Longitudinal sternal ballistocardiogram. The arrows indicate in order: the presystolic footward stroke, the first group of higher frequency oscillations in time with the first heart sound, and the second group of higher frequency oscillations in time with the second sound.

It is believed that this tracing follows the activity of the heart considerably more closely than the standard ballistocardiogram. In fact, the pattern resembles the typical form of the apex cardiogram.[6,7] The first systolic headward stroke occurs at the time of the isometric contraction of the ventricles. The systolic footward stroke and the footward component of the low-frequency wave are synchronous with rapid and slow ventricular emptying. The headward component of this low-frequency wave coincides with ventricular filling. The

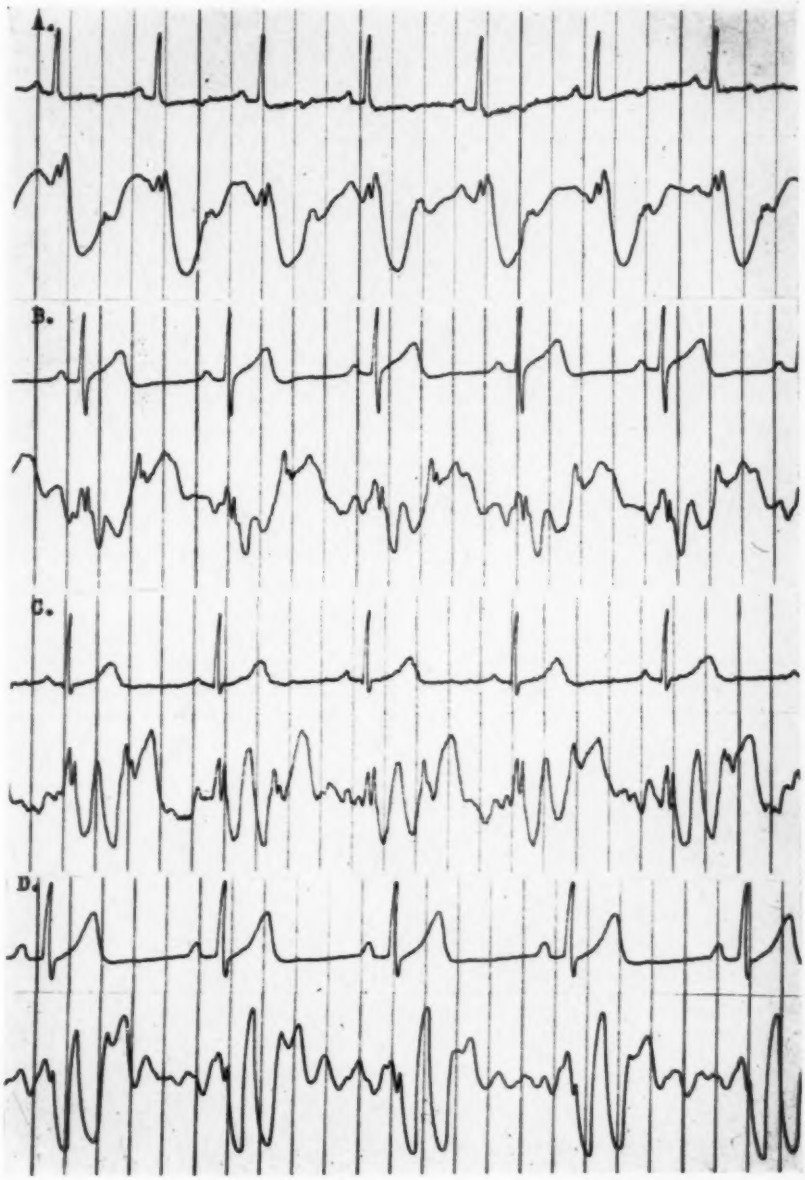

Fig. 4.—Longitudinal sternal ballistocardiograms. *A*, The cardiac pattern. *B*, *C*, and *D* show the appearance and gradual dominance of the "5" cycle waves.

two groups of higher frequency oscillations mark the time of the closing of both sets of heart valves. The presystolic footward stroke appears at the time of auricular systole.

In many cases respiratory oscillation of the base line requires breath holding or the introduction of an electronic filter which eliminates frequencies in the neighborhood of 0.3 cycle per second.

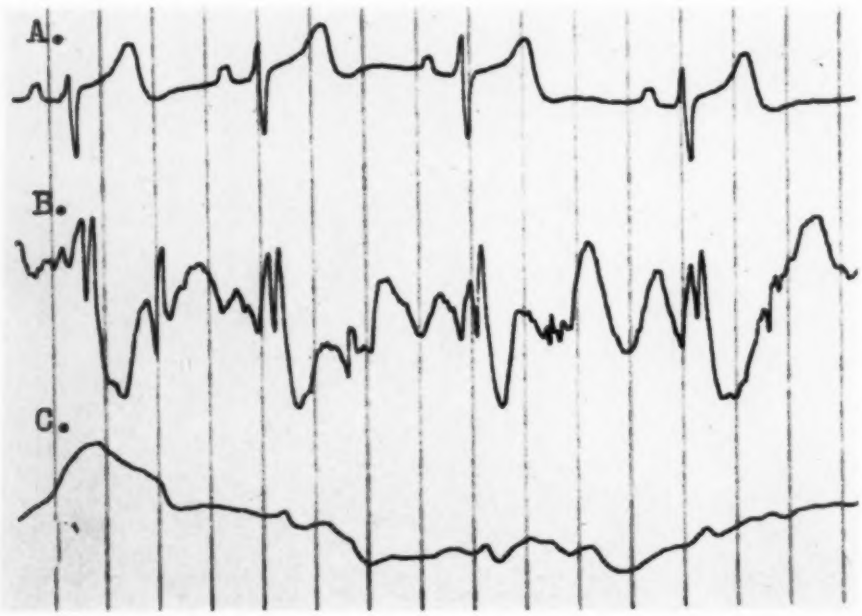

Fig. 5. Respiratory variation in the longitudinal sternal ballistocardiogram. Simultaneous tracings. *A*, Lead I of the electrocardiogram. *B*, The longitudinal sternal ballistocardiogram. In inspiration the cardiac pattern is evident. In expiration the "5" cycle waves are prominent. *C*, Respiration. Inspiration is up.

The remaining sternal records appear to represent combinations of the previously described sternal pattern and the superimposed standard ballistocardiogram. Selected sternal tracings in Fig. 4 have been arranged to show the transitions from the cardiac to the standard total body motion recording. A mid-systolic headward wave in the 5-cycle frequency range appears in these tracings. This headward wave varies from a small hump on the systolic component of the low-frequency wave to a wave which dominates the tracing. Where it dominates the tracing, waves in the 5-cycle frequency range appear in diastole as well. Such a pattern occurs in only 14 per cent of the cases. The 5-cycle waves diminish in amplitude in inspiration and increase in expiration (Fig. 5).

It is worthy of note that in the few patients with abnormal hearts whose thoracic tracings have been recorded, the longitudinal sternal tracing has a repetitive pattern even though the standard ballistocardiogram is totally unrecognizable (Fig. 6).

The lateral sternal tracings tend to follow the pattern of the longitudinal sternal tracings (Fig. 3). There are, however, amplitude variations. The low-frequency systolic wave is invariably leftward and the diastolic wave rightward.

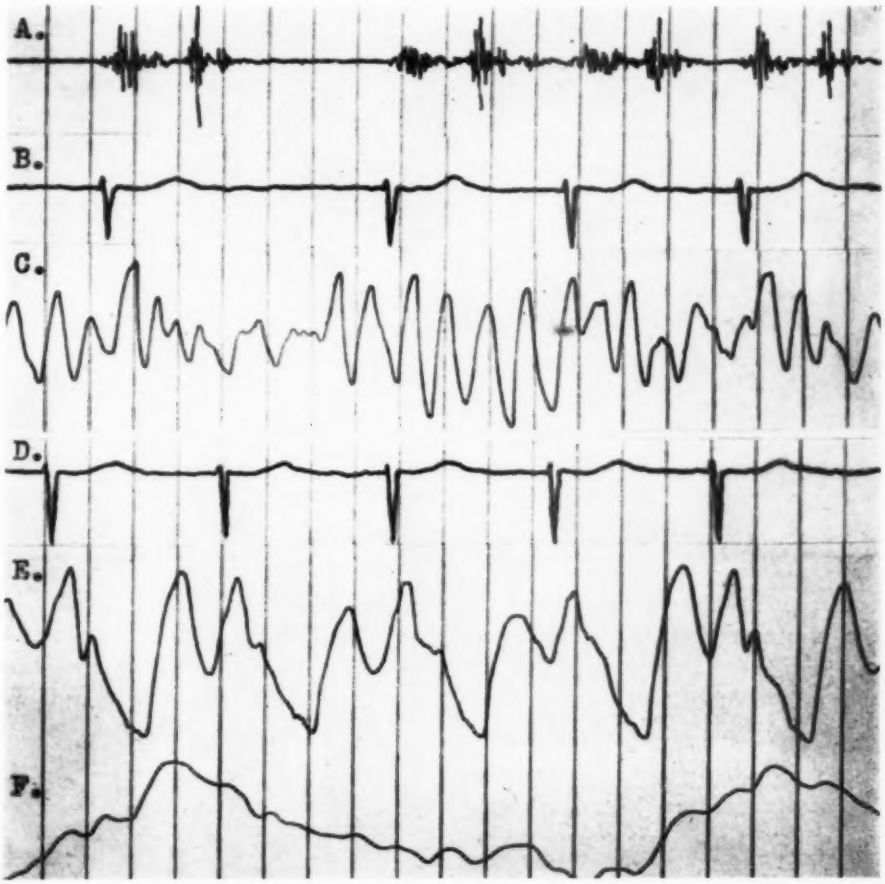

Fig. 6.—Longitudinal sternal ballistocardiogram from a patient with mitral stenosis and insufficiency with a tremendous heart and auricular fibrillation. Simultaneous supine tracings. *A*, Heart sounds from the apex. *B*, Lead I of the electrocardiogram. *C*, Standard ballistocardiogram from the legs showing a totally irregular pattern. Simultaneous prone tracings. *D*, Lead I of the electrocardiogram. *E*, Longitudinal sternal ballistocardiogram showing a repetitive pattern. *F*, Respiration. Inspiration is up.

DISCUSSION

The interscapular method of recording only partly enhances the effect of cardiac activity on the ballistocardiogram. Higher frequency oscillations related to valve closure are present in many tracings. These oscillations appear because the transducer is placed close to the origin of activity.

The interscapular records show another higher frequency phenomenon, the bi-peaked equivalent of the J wave. This phenomenon is similar to the bi-peaking described by Starr and Friedland[8] in a tracing from a patient with bundle branch block. They considered that asynchronous contraction of the ventricles

resulted in asynchronous recoil from deceleration of blood as it changed direction at the bifurcation of the pulmonary artery and at the arch of the aorta. In the present series, using normal subjects, there is no such asynchrony of ventricular ejection. Yet, there does remain a difference in arrival time between blood traversing the short pulmonary artery to its bifurcation and blood traversing the longer segment of the aorta to the peak of its arch. The proximity of the transducer to the source of these forces permits demonstration of these separate phenomena. In the main, however, the dominant waves of the interscapular tracings are in the frequency range of the natural resonant frequency of the body.

The sternal method of recording more successfully enhances the effect of cardiac activity on the ballistocardiogram. The heart and sternal region seem to have been sufficiently dissociated from the aorta and main body mass movements, in one-third of the cases, to produce a tracing which more directly reflects cardiac activity. In these tracings both low and high cardiac frequencies are reproduced.

Although the dissociation in the other two-thirds of the cases is not sufficient to damp out aortic and body mass waves, these tracings illustrate the transition from the standard aortic-body mass pattern to the cardiac-sternal mass pattern. The degree of dissociation may be, in part, related to the degree of flexibility of the costovertebral joints.

At present, this lack of dissociation in these cases constitutes a major problem in studying cardiac-sternal mass activity. The dissociation is somewhat increased in inspiration, perhaps due to the damping effect of increased lung masses. This increase in dissociation, however, is not sufficient or constant enough to solve the problem. A more satisfactory solution has been developed which will be presented in another paper.

One of the most provocative findings in this study is the distinguishable pattern of sternal tracings in patients with heart disease where the pattern of the standard ballistocardiogram is unrecognizable. This findings suggests that such an abnormal standard tracing is not entirely due to abnormal cardiac activity.

SUMMARY

1. The effect of cardiac forces on the ballistocardiogram has been enhanced by obtaining tracings from the interscapular and sternal regions.

2. The longitudinal interscapular tracing shows higher frequency phenomena related to the closing of the heart valves and to the recoil of blood in the aorta and the pulmonary artery.

3. The longitudinal sternal tracing shows a pattern which appears to follow cardiac activity more closely than does the standard ballistocardiogram.

4. The longitudinal sternal tracings from patients with heart disease show a distinguishable repetitive pattern even though the standard ballistocardiogram is totally unrecognizable.

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PROVOCATIVE ASPECTS OF LIPOTROPIC THERAPY IN ANGINA PECTORIS

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EXPERIMENTAL and clinical studies of the problem of coronary atherosclerosis have emphasized among other factors the particular role of cholesterol metabolism. In man and in animal experiments hypercholesterolemia, either as a sustained phenomenon or as recurrent episodes, has been correlated with the progression of atherosclerotic lesions.[1-4] Further evaluation has revealed, however, that many cases of coronary atherosclerosis have failed to show hypercholesterolemia. Attention has been directed, therefore, to the physical state of cholesterol in the blood as a factor in the pathogenesis of atherosclerosis.[5,6] Of particular interest currently is the relationship of the major components of the serum lipids, cholesterol and phospholipids; for the latter may presumably exert a stabilizing influence on the colloidal state of cholesterol in the blood. Emphasis has been placed especially on the serum cholesterol and serum phospholipid ratio as an index of this physicochemical phenomenon.[7-12] As a corollary of this hypothesis attempts have been made to treat coronary atherosclerosis and its clinical manifestations by means of lipotropic agents, and reduction of serum cholesterol levels relative to an increase in serum phospholipid concentrations has been regarded by some investigators as a beneficial change.[13]

On the other hand, some doubt may be expressed regarding the significance of the serum cholesterol - serum phospholipid ratio as an index of coronary atherosclerosis; for preliminary studies in this laboratory have indicated that an increase in this ratio has not been associated with aggravation of clinical coronary disease. This increase in ratio, rather than the allegedly therapeutic decrease in ratio, may be accomplished by a decrease in serum phospholipids relative to serum cholesterol, through the administration of Granulestin,* a concentrate of purified soy phospholipids consisting of lecithin, cephalin, and lipositol. This study was undertaken, therefore, to evaluate critically the effect of Granulestin in a group of patients with angina pectoris, both with respect to clinical course and serum chemical changes.

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METHODS

A group of patients with angina pectoris was selected for study from subjects regularly attending the cardiac clinics for over one year. Clinical evaluation included, in addition to physical examination and routine laboratory tests, electrocardiogram and ballistocardiogram, heart size mensuration by chest x-ray or orthodiagraphy, and serum cholesterol and serum phospholipid determinations in duplicate. The electrocardiograms were inscribed by means of a Sanborn direct-writing apparatus. The ballistocardiograms were recorded by means of a Glennite ballistocardiograph using the Dock shin-bar technique. Cardiac mensuration was made by measuring transverse diameter of cardiac silhouette in relationship to the predicted diameter for height and weight. Fasting serum cholesterol determinations were made as lipid phosphorus by the method of Youngburg and Youngburg, with the normal range of 6 mg. per cent to 14 mg. per cent, and the estimation of the serum phospholipids was made by using the conversion factor of 25 to express lipid phosphorus as phospholipid, with a normal range of 150 mg. per cent to 350 mg. per cent.

After initial evaluation was completed, only those subjects were selected for this study who had a valid history of angina pectoris together with evidence of heart disease in both the electrocardiogram and ballistocardiogram. Moreover, these subjects had no other major diseases that might have complicated the clinical picture except for moderate hypertension. Whatever medication the patient had been taking prior to this study was continued. Granulestin was given in doses of one heaping tablespoonful per day, or about 20 Gm. This dose was apparently the optimum, as suggested by previous studies. Thereafter, the subjects were checked once monthly for evaluation of clinical course and for repeat analyses of serum cholesterol and serum phospholipids. Repeat electrocardiograms and ballistocardiograms were made during the period of observation, which ranged from three to five months.

RESULTS

Although a large number of patients were started on this program, only twenty-five cases adhered to the requirements of the study. This group had an age range of 57 to 71 years, with a mean age of 64.4 years; sixteen patients were men and nine were women. Among these cases three subjects were Negro and the remaining twenty-two patients were white. Obesity was not a characteristic of this group, for only nine patients were moderately obese. Hypertension was not a prominent feature, for only eight patients had a moderate increase in blood pressure. The history of angina pectoris ranged from one to ten years, with a mean duration of 4.3 years. Anginal episodes requiring sublingual nitroglycerine tablets varied in incidence from several times per week to several times per day, with a mean incidence of five episodes per week. Only seven subjects manifested cardiac enlargement. Electrocardiograms were abnormal in all cases and included two healed myocardial infarctions, two left ventricular hypertrophy patterns, and one case of left bundle branch block. Ballistocardiograms were all abnormal, but only a few records showed the low

bizarre waves of the grossly abnormal pattern. Initial serum cholesterol levels were averaged from duplicate determinations and ranged from 155 mg. per cent to 362 mg. per cent, with a mean level of 235 mg. per cent, close to the upper limit of normal of 240 mg. per cent. Initial serum lipid phosphorus levels, similarly averaged, ranged from 5.9 mg. per cent to 16.2 mg. per cent, with a mean level of 9.6 mg. per cent, close to the average normal level for serum lipid phosphorus. These lipid phosphorus values corresponded to a range for serum phospholipids of 148 mg. per cent to 405 mg. per cent, with a mean value of 240 mg. per cent.

Granulestin was then administered to the patients, who were subsequently rechecked at monthly intervals. In six cases, or in 24 per cent of the group, some clinical amelioration was apparent in that the mean number of anginal episodes requiring nitroglycerine tablets decreased from 7 times per week to 2.5 times per week. When clinical improvement occurred, it did not appear promptly, but only after about one month of treatment. Moreover, once treatment was discontinued, the clinical state returned to the pretreatment picture in irregular fashion, in some instances over a period of several months. In this group, moreover, no change was evident on physical examination and in the electrocardiogram. Moreover, no change was evident in the ballistocardiogram, although one patient did manifest some improvement in that the still abnormal pattern became somewhat more uniform.

TABLE I. CHANGES IN SERUM CHOLESTEROL CONCENTRATIONS (MG. PER CENT) DURING LIPOTROPIC THERAPY IN SUBJECTS SHOWING CLINICAL IMPROVEMENT

SUBJECT	INITIAL VALUE	MONTHS OF TREATMENT			
		1	2	3	4
E.H.	288	275	232	254	260
C.K.	203	200	187	190	180
C.J.	255	195	208	237	248
F.S.	321	309	300	302	254
O.S.	216	227	215	230	220
P.M.	377	310	348	268	320
Mean value	277	253	248	247	247

Similarly, changes in serum cholesterol and serum lipid phosphorus levels were not striking, as presented in Tables I and II. In these tables values are given for only four months of therapy, for after the fourth month there was an irregular return to pretreatment concentrations. In the six patients manifesting clinical improvement the serum cholesterol decreased from an initial mean value of 277 mg. per cent to a terminal mean value during the course of treatment. The maximal decrease in these values, therefore, was only about 11 per cent. The serum lipid phosphorus, however, showed a greater decrease, for the initial mean value of 10.3 mg. per cent decreased to a final mean value of 7.5 mg. per cent, with a low mean value of 6.8 mg. per cent during course of treatment.

TABLE II. CHANGES IN SERUM LIPID PHOSPHORUS CONCENTRATIONS (MG. PER CENT) DURING LIPOTROPIC THERAPY IN SUBJECTS SHOWING CLINICAL IMPROVEMENT

SUBJECT	INITIAL VALUE	MONTHS OF TREATMENT			
		1	2	3	4
E.H.	8.9	7.5	6.6	5.6	6.0
C.K.	7.3	6.9	6.1	5.1	4.2
C.J.	9.1	6.9	8.8	5.9	6.0
F.S.	12.2	10.0	9.3	6.2	8.2
O.S.	9.7	8.4	6.1	8.7	9.0
P.M.	14.9	8.3	7.9	9.5	11.4
Mean value	10.3	8.0	7.5	6.8	7.5

These values would correspond to mean serum phospholipid levels of 258 mg. per cent initially, 188 mg. per cent terminally, and 170 mg. per cent as lowest value. The maximal decrease in serum phospholipid values was, therefore, about 34 per cent, or a response about three times as marked as that observed for the serum cholesterol. As a result of the relatively greater decrease in serum phospholipid values, the ratio of serum cholesterol to serum phospholipid showed a definite increase, as is evident in Table III. This maximal decrease in these concentrations did not persist for long, for once the decrease became apparent it only lasted for about three months before there was an irregular and gradual return to pretreatment levels. In only one case did the decrease persist for more than four months after it first became apparent, the number of anginal episodes requiring nitroglycerine tablets decreased from fifteen per week to five per week, and the ballistocardiogram manifested a somewhat more regular pattern.

TABLE III. CHANGES IN SERUM CHOLESTEROL—SERUM PHOSPHOLIPID RATIO (PER CENT) DURING LIPOTROPIC THERAPY IN SUBJECTS SHOWING CLINICAL IMPROVEMENT

SUBJECT	INITIAL VALUE	MONTHS OF TREATMENT			
		1	2	3	4
E.H.	129	147	140	181	173
C.K.	111	116	123	150	171
C.J.	112	114	95	160	165
F.S.	110	123	129	195	124
O.S.	89	108	141	105	98
P.M.	101	149	176	112	112
Mean value	108	126	133	145	131

In the remaining nineteen cases that failed to show significant clinical improvement, the mean serum cholesterol value was 226 mg. per cent initially, and 216 mg. per cent terminally, with a low value of 201 mg. per cent during treatment, or a maximal decrease of 11 per cent. The mean serum lipid phosphorus value was 9.9 mg. per cent initially and only 7.8 mg. per cent terminally,

which was also the lowest mean value during treatment. These values corresponded to serum phospholipid levels of 247 mg. per cent initially and 195 mg. per cent terminally. The maximal decrease in serum phospholipid values was, therefore, 21 per cent, or a response again about twice as marked as that seen for the serum cholesterol.

The differences between the two groups, the six cases with clinical improvement, and the nineteen cases without improvement, were essentially those of degree (Table IV). Although both groups manifested decrease in serum cholesterol and serum phospholipid levels, the decrease in the latter was more marked than in the former; and the group showing clinical improvement manifested a somewhat greater decrease in serum phospholipid values. It appeared to be difficult, however, to anticipate which subjects would manifest clinical improvement, for there was no significant difference between the two groups clinically, and indeed the chemical differences between those who improved and those who did not were slight.

TABLE IV. COMPARISON OF MEAN SERUM CONCENTRATIONS OF CHOLESTEROL, LIPID PHOSPHORUS AND PHOSPHOLIPID AND OF MEAN C-P RATIOS* BETWEEN THE GROUP SHOWING CLINICAL IMPROVEMENT AND THE GROUP NOT SHOWING IMPROVEMENT

MEAN SERUM VALUES (MG. PER CENT)	GROUP SHOWING IMPROVEMENT	GROUP NOT SHOWING IMPROVEMENT
Initial cholesterol	277	226
Terminal cholesterol	247	216
Lowest cholesterol	247	201
Initial lipid phosphorus	10.3	9.9
Terminal lipid phosphorus	7.5	7.8
Lowest lipid phosphorus	6.8	7.8
Initial phospholipid	258	247
Terminal phospholipid	188	195
Lowest phospholipid	170	195
Initial mean C-P ratio (%)	108	91
Terminal mean C-P ratio (%)	131	111

*Ratio of serum cholesterol to serum phospholipid, expressed in terms of per cent.

DISCUSSION

This study suggests that the use of lipotropic agents may temporarily ameliorate the course of some cases of angina pectoris and may effect a rather moderate transitory decrease in the serum cholesterol and serum phospholipid concentrations. But the subjects that may show some favorable response to this type of lipotropic therapy cannot be readily selected before treatment, and the improvement may be more apparent than real. Of particular interest is the fact that the lipotropic agent employed effects a greater decrease in serum phospholipids than in serum cholesterol. Such a change implies that the serum cholesterol-serum phospholipid ratio actually increases as a result of this treatment, a response that is just the reverse of what some students of cholesterol metabolism

have considered to be the desirable therapeutic effect. It is, therefore, most interesting and somewhat provocative that these changes have not been associated with any deterioration in the clinical course of patients studied in this group. Indeed, several individuals may have shown clinical improvement despite these "adverse" chemical changes. One may challenge, therefore, the significance of the serum cholesterol - serum phospholipid ratio even on clinical grounds. Jackson and Wilkinson[14] have doubted the usefulness of this ratio. DeWind[15] and his associates have failed to find a correlation between these lipid fractions and atherosclerosis. Rose and associates[16] have indicated how the serum cholesterol - serum phospholipid ratio may be invalid in the light of the relative distribution of the alpha and beta lipoprotein fractions. The variability of the serum lipid fractions in coronary disease as compared to normal controls was shown by Goldbloom.[17] In the light of this study, therefore, it is believed that the serum cholesterol - serum phospholipid relationship is of rather doubtful value. Indeed, other studies have indicated that more significant than chemical concentration of serum lipid components are the physical and colloidal states of the molecular aggregates constituting the serum lipoproteins.[18,22]

A second issue raised by this study is the fact that the decrease in serum cholesterol or phospholipids cannot be maintained for a long period of time. The decrease in serum concentrations appears within one or two months of treatment, and this effect usually regresses after about three months of further treatment. This response certainly suggests that the metabolic activity of the body adapts itself to whatever modifying influence may be introduced by the lipotropic agent. Such a response, furthermore, is consistent with the fact that cholesterol and other components of the lipid structures are synthesized by the body to meet the lipid requirements of tissue cells and tissue fluids. To meet these requirements, it is altogether likely that metabolic activity circumvents the effect of lipotropic agents in due time. The effect of lipotropic agents, therefore, may be transitory in most subjects. Perhaps it is this transitory effect that has given rise to differences of opinion regarding the chemical effect of lipotropic agents. As a corollary of this study, it is essential to check blood chemical determinations for four or five months of therapy before any conclusion may be made regarding the effect of lipotropic agents.

A third item in question lies in the apparent fact that the various lipotropic agents available may influence different components of the total serum lipid structure. For although various agents have been alleged to modify serum cholesterol levels at least temporarily, the agent employed in this study appears to manifest a greater effect on the serum phospholipid concentrations.

Another controversial issue regarding the use of lipotropic agents rests on the duration of treatment. This study indicates that treatment may be intermittent, perhaps for about four months at a time, with the first month utilized to induce a change if such a change will occur and with the next three months utilized to maintain this change. Thereafter, lipotropic therapy may be discontinued for the next several months, in view of the fact that the metabolic activity of the body appears to reverse whatever effect has been achieved on the cholesterol and phospholipid complex.

Finally, the question arises how lipotropic therapy may have benefited even a small percentage of the cases of angina pectoris so treated. Although several patients have felt better on this treatment, no definite objective changes have been apparent on physical examination, electrocardiogram, or ballistocardiogram. It is, therefore, unlikely that any structural change occurred in the myocardium or in the coronary arteries as a result of this treatment. If lipotropic therapy alters the total serum lipid structure and particularly influences the physical state of the lipoprotein complex, however, such a change may improve coronary artery blood flow by lessening local vascular resistance, without regression of the structural abnormality.

SUMMARY

1. A group of twenty-five patients with angina pectoris were evaluated before and during a course of lipotropic treatment with Granulestin, a soy lecithin preparation, and six subjects (24 per cent) appeared to improve on this program, even though very little objective change was evident in their cardiac status.

2. Serum cholesterol levels decreased only slightly during treatment, serum phospholipid concentrations decreased rather definitely to effect an increase in the serum cholesterol - serum phospholipid ratio, a change which may be considered provocative in that no subject became worse and indeed some appeared better.

3. These chemical changes were rather similar both for the patients who manifested clinical improvement and for those who did not. In general these changes were maintained for three or four months and then regressed in irregular fashion.

4. The tendency for serum cholesterol and serum phospholipid values to return to pretreatment concentrations despite continued therapy suggests that lipotropic agents, if apparently beneficial, should be used for only several months at a time.

5. The controversial issues of this study are discussed in the light of current theory.

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FLARIMETER TESTS ON ATHLETES

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THE flarimeter[1-4] is a clinical instrument for testing circulatory fitness. The subject blows through a standard orifice at a standard pressure. The examiner can follow blood pressure or pulse rate during the blow to measure the circulatory response. Two orifices are provided. One is large enough to empty the lungs and so measure vital capacity. The other, a small orifice, provides for a standard method of holding the breath.

The athletes at Princeton University give reliable criteria for the normal individual. These men are carefully selected, given a medical examination before being admitted to each sport each season, are then watched closely by the coach and also by each other to make sure that they do not break training, and finally demonstrate their fitness frequently by athletic performance. Such men represent a standard that few ordinary normal individuals approach. The present study attempts to interpret flarimeter responses in these athletes.

To check for staleness, 104 members of the crews were examined the first year, but not enough information could be obtained on each man for a demonstration. The next year thirteen of the varsity heavy crew volunteered for weekly tests. Similar methods were applied to the basketball team for a season. These sports, however, do not provide unambiguous objective evidence of individual performance. So the main study has been limited to swimmers and runners who have individual records. Even these are not strictly comparable.

STANDARD STIMULUS

Whatever the technique adopted for a functional test, it is essential to keep it standard. Then the data refer to definite conditions. Interpretation becomes specific, records brief. Examiners agree because they observe the same phenomena. The data show the state of the person examined, not a mixture with extraneous effects of unspecified variations in technique.

For the first test on an athlete the standard technique developed for insurance examination could not be improved upon, except in one particular. Told to blow as long as possible through the small orifice, beginning 10 seconds after exercise, he had to decide when to stop, so subsequent responses were not standard. For example, one man (R8) held this blow 76 seconds, but the schedule requires blood pressures to be taken one minute after exercise and he was still blowing. It was decided, therefore, to tell the athlete to hold this blow until told to stop at 30 seconds.

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By fixing the length of this blow, subsequent responses become independent of the will of the subject, repeated tests strictly comparable. The combination of this standard blow with Master's standard exercise[5] constitutes a stimulus to the circulation which gives reproducible, characteristic, and accurately observable responses. Changes in physical condition are reflected in the rise in systolic pressure. To show this the varsity oarsman (R8), mentioned previously, volunteered for the following experiment. He was given the same exercise, 21 ascents in 90 seconds, in three successive tests 15 minutes apart. Exactly 10 seconds after each exercise a small-orifice blow was started and stopped, respectively, at 20, 30, and 40 seconds. The systolic rise, observed exactly one minute after exercise, gave the respective values 34, 40, and 46 mm. Hg.

Standard Technique For Flarimeter Tests

Test I
Pulse Rate
Systolic Pressure
Diastolic Pressure (4th point)

Test II *Repeat*
Vital Capacity
Seconds×0.2=Liters

Test III *Blow 3.*

Min.	Seconds	*Time Schedule*
0		30-50 **Systolic** Pressure
		Deflate—Record
0	55-60	**"Inspire!"**
0	60	**"Blow!"**
1		10 Inflate—**T20** in seconds
		Maximum Systolic
		Total Length of Blow
		Deflate—Record
		Repeat as in blow 3, that is —
2		30-50 **Systolic** Pressure
		Deflate—Record
		etc. Begin blow 4 at 3 min.

Test IV
Pulse Rate, 30-45 sec. after end of blow
Systolic Pressure, 60" " " " "
Diastolic Pressure (4th point)

Test V

Min.	Seconds	*Time Schedule*
0	0-60	} Standard exercise for 90 sec.
1	0-30	} See table for number of ascents
		Record " "
1	35-40	**"Inspire!"** (*Blow 5.*)
1	40	**"Blow!"** Record length
		Stop this blow at 20 sec. (30 sec. for athletes)
2		30-60 **Systolic** and **Diastolic** Pressures Deflate—Record
3		0-15 **Pulse Rate** Record
		Repeat as in Test III, that is —
3		30-50 **Systolic** Pressure
		Deflate—Record
		etc. Begin blow 6 at 4 min.

Short Test—Omit III & IV; that is, give I, II, and then V. If length of final blow (No. 2) is less than 40 seconds, T20 less than 25 seconds, or Diastolic (in mm.) or Pulse-Rate (in beats per min.) in V is 8 or more above its value in I, give III & IV and repeat V (blows 3, 4, 5, & 6). Base S=120 D=78 R=52

(Record after Test II also No. of ascents)

Name S 141 Age 19 Sex M Occupation Sprints Ht. 5 ft 10¼ ins. Wt. 157

	I		II	III		IV		V				
	At Rest		Vital Capacity	Blows with Small Orifice	3	At Rest		Exercise Small Orifice Blow	1	5	Small Orifice Blow	2 6
R_o =	Pulse Rate	55	Sec	Systolic	(120)	Rate	47	No. Ascents	24		Systolic	(120)
S_o =	Systolic	124	1 24	To (sec.)	20	Systolic	122	Length of Blow, Sec.	30		To (sec.)	13
D_o =	Diastolic	78	2 28	T20 Seconds	50	Diastolic	76	Systolic end 1 min. S_1 =	154	34	T20 Seconds	35
$P_o = S_o - D_o$ =		46	3	Maximum Systolic	142		46	Diastolic end 1 min. D_1 =	82	4	Maximum Systolic	150
			Liters	Length of Blow, Sec	51			Pulse Rate end 1½ min. R_2 =	40		Length of Blow, Sec.	45
$F_o = \frac{46 \times 55}{100}$ =		25	%119	S+	22	F = $\frac{46 \times 47}{100}$ =	22	S_2 =	148	28	S+	30

Remarks: T > 40 $P' = \frac{P_1 + P_2}{2} = \frac{72+70}{2} = 71$ D_2 = 78 0 T = 31

$F' = \frac{71 \times 40}{100} = 28$

$100(\frac{F'}{F} - 1)$ = Increase = 27%

Fig. 1.

The decision to standardize the blow at 30 seconds for the athletes was reached with some trepidation, for only 49 per cent of the crew attained 30 seconds in the first 200 tests when asked to blow as long as possible (6 per cent reached 50 seconds); yet when told to blow until told to stop, which would be at

30 seconds, more than 98 per cent of the athletes met this demand. It has proved to be, therefore, a successful standard stimulus for athletic men. A sample first test on a good swimmer is shown in Fig. 1.

Standard stimulus possesses the advantage over standard exercise not followed by a flarimeter blow that the response is mostly in systolic pressure. Thus, the first thirty-one varsity swimmers gave medians at peak of training (selected tests) showing an average rise in diastolic pressure, one minute after exercise, of 2 mm. Hg compared with 21 mm. Hg in the systolic pressure. Heart rate 1½ minutes after exercise averaged 2 beats per minute below the rate before exercise. For this reason electrocardiograms after standard stimulus are more valuable than after the exercise alone. It is known, for example, that increase in heart rate in itself tends to depress the S-T junction or segment of the electrocardiogram. This interferes with the use of S-T depression as a test of coronary insufficiency after exercise. Standard stimulus, however, is relatively free from this disadvantage, for the blow produces a powerful vagus stimulation which prevents the increase in rate.

FLARIMETER TOLERANCES

Instead of observing the systolic rise in blood pressure during a flarimeter blow it is more accurate and convenient to measure on a stopwatch the seconds required for a given systolic rise. These times are called "flarimeter tolerances." For example, "T_{20}" is the time (in seconds, measured from the beginning of the blow) required for the systolic pressure to rise 20 mm. Flarimeter tolerances usually run parallel with T_m, the maximum length of blow; but unlike T_m, these tolerances are independent of the will of the performer.

Most of the athletes reach T_{40} without too much effort, so that by stopping the blows routinely at T_{30} we avoid the emotional reactions involved in pushing blows to the limit. The two outstanding characteristics of an athlete in these tests are a slow heart rate and large flarimeter tolerances. The frequency distribution of T_{20} in 281 tests on 104 athletes is compared with that of 1,303 tests on ordinary normal individuals in Table I. Nearly one-half of the athletes gave T_{20}'s of 45 seconds or more, which is over three times the frequency of such slow responses in the ordinary normal individuals.

TABLE I. COMPARISON OF FLARIMETER TOLERANCES: 281 TESTS ON 104 PRINCETON CREW (ONE EXAMINER) VS. 1,303 FIRST-CLASS MALE INSURANCE APPLICANTS BY 21 SELECTED EXAMINERS

T_{30}	NO. TESTS		%		CUMULATIVE %	
(SEC.)	CREW	APPS.	CREW	APPS.	CREW	APPS.
Under 25	18	148	7	12	7	12
25–34	56	433	20	35	27	47
35–44	63	468	23	38	50	85
45 and over	138	194	50	15	100	100
Total with T_{20}	275	1,243	100	100		
T_{20} not reached	6	60				

Later experience has confirmed these results, nor are they confined to the crew. Nearly one-half of the tests give a T_{20}, at least 50 seconds, and one in seven reaches 60; but there is an enormous range. One cannot say that any man with a long T_{20} will be a good athlete, or that every champion must have a long T_{20}, any more than that they must have a slow pulse. All we can say is that a slow flarimeter response and a slow pulse suggest an athlete, just as his physique does. Apparently each man starts with a characteristic heart rate and flarimeter tolerance; by the time he becomes a college athlete these have been modified by years of training.

ABDOMINAL CONTRACTION

A backstroke swimmer in good condition had his appendix removed in the middle of a swimming season. After leaving the hospital, three weeks later, his rectus abdominis muscles were quite inert, he had a little potbelly, and T_0 had risen from 20 to 40 seconds. A compression band containing a rubber bag for inflation was tied about his waist to support the abdomen. But a steady compression of 50 mm. Hg had no effect on his T_0, in fact it increased to 49 seconds. The same test with a compression of 100 mm. given five other swimmers, all in good condition, also produced a negligible median increase in average T* of 1 ± 2 seconds. Six weeks after appendectomy our backstroke was again in form, winning his event, his potbelly had vanished, and his T_0 had returned to 14 seconds. This shows that the tolerance T_0 measures abdominal pooling.

During a flarimeter blow the systolic pressure is sometimes seen to surge upward suddenly, then drop back a little. Observed closely, each such jump in systolic pressure follows a jerk in the abdominal muscles. They can be produced at will. If the subject contracts suddenly on signal it is almost always effective in producing a jump in systolic pressure. To determine the effect of abdominal contraction on flarimeter tolerances, sixteen athletes were asked to blow, first without, then with contractions at 30, 45, and 60 seconds. Their average T was shortened 5.2 ± 0.2 seconds. The following technique has therefore been adopted as routine. Whenever T_{20} exceeds 45 seconds the subject is instructed to contract on signal at 45, relax gently at 50, and contract again suddenly at 60 seconds.

This technique does not effect T_0, for its sluggish border is 30 seconds. Median T_{20} exceeds 45 and median T_{30} is about 60, which is why these times were chosen. The surge in systolic pressure resulting from the first contraction usually brings on T_{20} but not T_{30}, which often follows the second contraction. The technique tends to concentrate the T_{20}'s about the median, to shorten the T_{30}'s, and to eliminate freak responses which upset the statistics. If, in spite of such contractions, T_{20} exceeds 60 seconds, one must assume that this sluggish response is characteristic.

RESPONSES TO STANDARD STIMULUS

The increase in systolic pressure (including the 30 minute blow begun 10 seconds after exercise in this interval) 1 minute after exercise is given in Table II. Fifty runners are compared with 105 athletes, which include also 11 crew,

*Average T is defined as one-third the sum of T_0, T_{20}, and T_{30}.

12 basketball, and 32 swimmers. The systolic pressure rose less than 20 mm. Hg in 61 per cent of the 1,303 applicants for insurance, but only 5 per cent of them blew as long as 30 seconds. It reached 35 mm. Hg in 5 per cent of them compared with 12 per cent of the athletes in Table II. There is no doubt, however, that if the applicants had by a tour de force accomplished a 30-second blow their systolic responses would have been much greater than those of the athletes.

TABLE II. RESPONSES TO STANDARD STIMULUS: STANDARD EXERCISE PLUS 30-SECOND BLOW

	NO. OF TESTS		% OF TESTS		CUMULATIVE %	
SYSTOLIC RISE (MM. HG)	50 TRACK	105 ATHLETES	50 TRACK	105 ATHLETES	50 TRACK	105 ATHLETES
Under 10	2	9	1	2	1	2
10–19	59	130	26	27	27	29
20–24	61	142	27	29	54	58
25–34	76	147	34	30	88	88
35–44	19	56	9	11	97	99
45 and over	7	9	3	1	100	100
Total	224	493	100	100		
PULSE RATE (PER MIN.)						
Under 40	2	5	1	1	1	1
40–47	25	68	11	14	12	15
48–55	80	156	36	32	48	47
56–63	68	164	30	33	78	80
64–71	33	77	15	16	93	96
72–79	13	23	6	4	99	100
80 and over	4	5	2	1	100	
Total	225	498	100	100		

The distributions of heart rate (R′) 1½ minutes after exercise are also given in Table II. Standard stimulus slows the pulse for a brief period, and the time schedule is arranged to count it near its minimum.* It is quite probable that this minimum rate for veteran athletes at peak of training averages about 50 beats per minute. There are no significant differences between the 50 track men and the whole group in either response.

The diastolic pressure is also below rest value for an interval after standard stimulus. Among athletes this minimum is usually more marked than among ordinary normal individuals. Nevertheless it may be higher; a rise of 8 mm. or more was reported in 9 per cent of the 1,303 first-class insurance risks of Table I. Such a rise was observed in 71 tests on 47 of the 105 athletes of Table II. Thus, nearly one-half the athletes show this rise once or twice, averaging about once in 7 tests. Obviously, therefore, a single such finding cannot be considered abnormal. Momentarily imperfect function can occur in the best of men at any time.

*Continuous direct-writing electrocardiographic records of Lead II confirm this.

The exercise test was standardized by Master and Oppenheimer[6] so that blood pressure (and pulse rate) normally returned to rest value in just two minutes. Standard stimulus has delayed this return by inserting the 30-second blow, so that the systolic pressure (S_2) taken 2 minutes after exercise should be slightly above its base (S). In fact, 65 per cent of the 105 athletes gave plus values of (S_2-S) of 10 mm. or more in at least one test, and such a rise was observed in 41 per cent of the tests on these 68 men. So an upper border of 15 mm. is rather severe for the athletes, for one in four reached this border in at least one test, while 9 per cent of the tests gave values of 15 mm. or more. Among ordinary normal individuals the percentage would be higher (if they could complete the 30-second blow).

A final small-orifice blow is begun 2½ minutes after exercise (more exactly 4 minutes after it started). The tolerances to this blow are about the same as those before exercise. In over one-half the tests, they differ by less than 5 seconds. The only effect, if any, appears to be a slight improvement. Standard stimulus seems to stabilize the circulation in athletes. For this reason tolerances to this blow will be adopted as standard, preferable to those before exercise.

FLOW INDEX

Five responses to standard stimulus can be combined rationally into an index number. Physiologists agree that the product of pulse pressure and pulse rate is a rough index of blood flow.* When changing rapidly, as after standard stimulus, pressure and rate must be observed simultaneously. In standard technique they are taken in succession; but the average of pulse pressures at 1 and 2 minutes after exercise approximates P′, its value at 1½ minutes, so that the product $F' = P'R'/100$ is the index desired.†

To show the variations in response to standard stimulus in individual athletes, two are compared in Table III, a champion swimmer with a hypertensive rower. The first was tested on 16 days over 4 years, the second on 6 days over 4 months in his senior year. The medians at rest are for 16 observations on each man, yet the average deviations of single observations (A.D.) are much larger for the rower in spite of the shorter period. Notice that his diastolic pressure is normal, it is his pulse pressure which is excessive, along with the resultant systolic pressure. His flow index at rest is more than two and one-half times that of the swimmer. It is hard to believe that metabolic demands could explain such a difference in flow.

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*For convenience we have defined the "flow index" (F) as $F = PR/100$, where $P = S - D$. P is pulse pressure, S systolic, and D diastolic, all in mm. R is pulse rate, in beats per minute. This product indicates minute volume assuming no change in arterial elasticity.[7,8]

†It combines S_1, D_1, R′, S_2, and D_2, all of which are observed directly. D_2, the diastolic 2 minutes after exercise, is an addition to standard technique, which calls only for S_2; but D_2 rarely differs significantly from the diastolic before exercise, in normal individuals. F′ measures flow relative to F, since arterial elasticity is the same when $D' = D$ (Table V).

TABLE III. CONSTANCY OF RESPONSE TO STANDARD STIMULUS—WORLD CHAMPION SWIMMER (S60) VS. HYPERTENSIVE ROWER (R33)

RESPONSE	MEDIANS		A. D.*		% A. D.*	
	S60	R33	S60	R33	S60	R33
At Rest						
Systolic (S)	115	150	3.9	6		
Diastolic (D)	77	72	3.8	6		
Pulse pressure (P = S-D)	37	78	4.4	7	12	9
Pulse rate (R)	56	74	4.2	5	8	7
Flow index (F = PR/100)	22	58	3.2	5	14	9
After Std. Stimulus						
Systolic (S′)	130	175	3.9	4		
Diastolic (D′)	75	74	4.4	7		
Pulse pressure (P′ = S′-D′)	52	101	7.6	6	14	6
Pulse rate (R′)	52	76	3.2	13	6	17
Flow index (F′ = P′R′/100)	28	77	3.2	11	11	14
Flarimeter Tolerances						
T_{20}	46	25	4.3	8	9	32
T	40	28	3.3	5	8	18
% Increase in flow [100(F′/F — 1)]	29	32	17	15	59	47

*A. D. = Average deviation

After standard stimulus the oarsman's diastolic pressure is stable and both diastolic and pulse rate are normal, although not the optimum response (a slight drop) shown by the swimmer. His pulse pressure and flow index have increased to excessive levels. Curiously, the per cent increases in flow index for the two men are almost equal. The rower's flow at rest is already too high, so this increase must be excessive also.

The worst variations in this man are in R′, the rate after stimulus. Before exercise the rate (R) is stable enough; but R′ varies from 64 to 100, with an A.D. of 13, more than four times that of the swimmer (almost three times in per cent A.D.). When given standard exercise alone his pulse rate fails to return, being 90 two minutes after. A cold pressor test showed hyper-reaction in diastolic pressure. His electrocardiogram (recumbent) showed a slight S-T depression in Leads II and III. In spite of his robust appearance, he seems to be a mild case of neuro-circulatory asthenia. Since he was an excellent oarsman, the coach wanted him, and he was allowed a brief period on the JV boat. Hard training reduced his blood pressure more than did Easter week in the sun on a Florida beach, although such an inference may ignore emotional factors. Finally, his flarimeter tolerances are not much more than one-half those of the swimmer, which are close to the medians for the athletes at peak of training. These circulatory responses are exaggerated like all the others. Every variable, at one point or other, shows over-response.

If the deviations in systolic pressures are assumed to be independent of those in diastolic, the expected A.D. in pulse pressure is the square root of the sum of the squares of the A.D.'s in its components. But three out of the four A.D.'s in pulse pressure are less than expected, indicating some tendency toward compensation. The same may be said for the flow index in terms of per cent A.D., three out of four are less than expected, assuming the per cent A.D.'s in pulse pressure and pulse rate to be independent. These results indicate some physiologic control in each of these variables, they are not mere mathematical artifacts. This is confirmed by our results on the other athletes. For example, 93 tests on twelve swimmers gave values of the product which varied from individual medians only one-half as much as expected, assuming components independent.

An example of a remarkably stable flow index after standard stimulus is shown in Table IV. Six tests on this athlete over a period of six years give an average deviation from the median index (F′) of 1.6 per cent. The expected value is 13 per cent. Notice the stabilizing effect of standard stimulus.

TABLE IV. STABILITY OF BLOOD-FLOW INDEX: TRACK ATHLETE (T57)

DATE	P	R	F	P′	R′	F′
5–25–49	38	60	23	45	64	29
3– 3–48	46	68	22	60	52	31
5–13–43	36	72	26	43	72	31
5–11–43	30	72	22	56	56	31
5– 5–43	34	66	22	51	60	31
4–20–43	44	60	26	54	56	30
Median	37	67	22	52	58	31
% A.D.	13	6	7	10	9	1.6

NORMAL STANDARDS

There is little point in using a mass of nondescript data to define the normal. A small series on carefully selected athletes yields results which are more significant. Table V gives medians of individual medians of tests at peak of training, as estimated from performance. First, thirty-one letter men were ranked in order of swimming ability by the coach. Medians for the top fifteen are given in column (1), those for all thirty-one in column (2). In column (3) are given medians for forty-nine other letter men tested since. Medians for eighty-eight track letter men (runners) are shown in column (5).

Deviations were computed of individual medians from the medians for the groups, and the medians of these (without regard to sign) are given in columns (4) and (6). They indicate that the differences between the groups are too small to have much significance although almost all are in the direction expected. The most remarkable feature of the individual medians is their narrow range. The champions are almost identical with the others. Here and there a good athlete shows a physiologic peculiarity which seems to have no relation to his ability.

TABLE V. NORMAL STANDARDS (MEDIANS AT PEAK OF TRAINING)

	80 VARSITY SWIMMERS				88 TRACK	
	TOP 15	31*	49 OTHER†	MEDIAN DEV. (31)	MEDIAN‡	MEDIAN DEV.
	(1)	(2)	(3)	(4)	(5)	(6)
At Rest—Sitting						
Systolic (S)	120	120	122	4	120	4
Diastolic (D)	78	76	78	6	76	4
Pulse pressure (P = S-D)	44	44	46	4	42	6
Pulse rate (R)	60	60	60	4	56	4
Flow index (F = PR/100)	25	26	27	2	24	3
After Std. Stimulus						
Systolic rise (S_1-S)	20	21	22	3	20	4
Diastolic rise (D_1-D)	2	2	0	2	0	4
Pulse rate (R′)	56	58	54	6	52	4
Systolic return (S_2-S)	4	4	10	3	8	4
Diastolic return (D_2-D)			0	3	0	2
Flow index (F′ = P′R′/100)	30	30	32	3	29	3
Flarimeter Tolerances						
T_0	20	18	17	2	17	3
T_{20}	48	49	45	4	46	8
T_{30}	62	62	54	4	54	7
T	44	44	39	3	39	6
% Increase in flow 100(F′/F-1)	20	21	21	9	18	13

*83 tests selected from 226
†Selected from 170 tests
‡Selected from 348 tests

Thus, the slowest median pulse (R′ = 44) among the thirty-one swimmers is shown by No. 9 in rank (although a distance track captain gave median R′ = 36). The shortest median tolerance (T = 35) among the thirty-one swimmers was No. 14, the longest (T = 68) was a champion, No. 2, but clearly a freak in breath-holding ability.

Two-thirds of the 168 athletes have a systolic pressure base nearest 120, one-sixth each nearer 110 and 130. There was much emotional fluctuation but seldom did it justify a change of base, except that a few freshmen showed a low pressure which rose 10 mm. by their senior year. The median deviations in S_1 and D_1 for the thirty-one men are just double those in (S_1- S) and (D_1- D), which suggests that about one-half the variation in S_1 and D_1 can be ascribed to changes in base.

It must be emphasized that this picture of good athletes represents them not under stress, as they would be when examined for a job, but in a cooperative mood of research. No penalty attached to the findings. Of course, they were curious and confessed to apprehensions. The tests were made in a warm dressing room just before the workout (4 to 5 P.M.), the athletes sitting at rest, relaxed, alone with the same examiner each time, and with only a mild curiosity concerning the result. Every effort was made to get them to relax. Times of stress were avoided, and tests showing emotion were not selected for the medians if other tests were available.

DISTURBING FACTORS

Most athletes have stable circulations, as is evident from Table VI. Of course, deviations depend on control of testing conditions as well as on fidelity to training. The tests on the crew and basketball team were unselected, one test each week on each man, those on swimmers and runners were taken from Table V.

TABLE VI. COMPARISON OF ATHLETES

No. Men	10	12	80	88	10	12	31	88
No. Tests	54	78	396	348	54	78	226	348
	MEDIANS OF INDIVIDUAL MEDIANS				MEDIAN DEVIATIONS			
	(VARSITY)				FROM IND. MEDIANS		FROM MED. MEDIANS	
	CREW	BASKET-BALL	SWIM-MERS	TRACK	CREW	BASKET-BALL	SWIM-MERS	TRACK
R	60	60	60	56	4	3	4	4
S_1-S	24	20	21	20	3	4	3	4
D_1-D	0	0	1	0	2	4	2	4
R′	54	54	56	52	3	2	6	4
S_2-S	6	4	6	8	2	3	3	4
T_{20}	56	51	46	46	6	6	4	8
T_m	82	72			6	3		
					FROM MEDIAN MEDIAN			
S	130	117	120	120	2	3	4	4
D	78	71	76	76	2	4	6	4
P	50	46	44	42	2	4	4	6
F	30	25	26	24	4	2	2	3
F′	35	30	30	29	2	3	3	3
+%	16	22	21	18	7	6	9	13
F′-F	5	6	5	5	2	2	2	4

Deviations of single tests from each individual's median were computed for crew and basketball, and the values shown are the medians of these (without regard to sign). They indicate how much these athletes vary from week to week. In contrast, for the swimmers and runners the deviations taken were of individual medians from their median for the group and the medians of these indicate how much these athletes differ from each other. The fact that these two types of variation are roughly equal suggests that both are largely emotional. Thus accurate observation on a rigorous time schedule shows an emotional factor superposed on quantitative physiologic effects.

Ordinarily, the flow index (F′) decreases from test to test, as familiarity lessens emotion; but when the athletes were first attached to the electrocardiograph (a new experience to most), F′ increased in eleven out of fourteen men, showing an increase in emotion. Median increases in P′, R′, and F′ were, respectively, 5, 4, and 5. Continuous records of Lead II showed sudden vagus slowing whenever the heart accelerated enough, most often toward the end of a flarimeter blow, but sometimes early in the blow or after it stopped. Ten men out of thirty-nine showed irregularities during or just after blows in 10 tests out of 49. These included 11 premature contractions (9 ventricular), 2 wandering pacemakers, and one atrioventricular block.

The most spectacular example of emotion was a freshman hurdler with a recumbent systolic pressure over 190 mm. Hg in February, 1941. He promised me a test but broke two appointments. On April 3, 1941 I caught him alone after a workout, the sweat pouring off him. He was so surprised that his systolic was only 140 mm. Hg that he was a willing subject thereafter. I told him to let me test him frequently to overcome emotion. He did, as shown in Table VII.

TABLE VII. LOSS OF FRIGHT: HURDLER (T34)–BASE 120 TO 74

	S	D	P	R	F	S′	D′	P′	R′	F′	INCREASE (%)	T	
1941													
4– 3	140	72	68	100	68	(After Workout)						27	
4–10	124	74	50	66	33	132	75	57	60	34	3	50	
4–21	120	74	46	60	28	(Injury 4-16)						38	
10– 7	122	78	44	72	32	140	82	58	56	32	0	38	
1942													
4–14	122	70	52	60	31	132	77	55	56	31	0	40	
	116	70	46	60	28	143	83	60	48	29	4	40	Accel.
4–30	110	70	40	60	24	120	73	47	52	24	0	42	
5– 5	110	80	30	52	16	118	76	42	44	18	12	44	Basal
	110	80	30	52	16	131	84	47	44	21	31	41	Accel.
5–26	114	80	34	56	19	124	81	43	48	21	10	44	

Tests were standard except those marked "Accel."; in these the 24 ascents were completed in 60 instead of the standard 90 seconds. In basal tests before breakfast (May 5, 1942) his recumbent blood pressure was 98 to 66 mm. Hg, nearly 100 mm. below his February, 1941, systolic pressure. Flarimeter tests were normal, but the cold pressor test (his first) was hyper-reactive (S rose 28, D rose 30). He passed his Air Force examination in April, 1942, for which he thanked me. In the Cornell meet (May 2, 1952) he won more points than any other man on the team.

The evidence cannot be presented briefly, but a careful study of 426 athletes in the past 20 years, many through their whole college careers and some even longer, has convinced us that the observed changes are real, depicting the actual condition when tested. Apparent discrepancies are usually due to emotion; but how could it be otherwise? We cannot function without an extremely complex

and sensitive nervous system, so we must expect the resulting vagaries. To avoid misinterpretation, repetition is essential. Judgment must be reserved and tentative, even when the data appear consistent and conclusive.

The best estimate of emotion is given by comparison of F′ with F. F should be below 25 and F′ below 30; but if F′ is less than F, the probable explanation is that there is an excessive flow at rest, due to emotion, even greater than the moderate demand of standard exercise, and that the stabilizing effect of standard stimulus has decreased the flow more than the increase required to clean up the oxygen debt. If previous tests are available, the whole circulatory picture may reveal the effect of emotion. It is when the attempt is made to discount disturbing factors that one appreciates a wealth of detailed standardized data. The more there is, the more reliable is the estimate of fitness.

CORRELATION WITH PHYSICAL CONDITION

No functional test can predict athletic performance with certainty. The naive notion that a formula will grind out a true score of fitness does not agree with experience. Not only is there more to the athletic event than what is tested; the event itself cannot predict its own repetition, as time-trials have shown. Experience has made the athlete uncertain of future performance, and this apprehension does not help his nervous coordination.

There seems to be a feeling in some quarters that endurance tests, such as the Harvard Step-Up Test,[9] circumvent the nervous system by massive muscular work; but the heart rate, which is used as a criterion, is even more labile than systolic pressure. Scores based upon it sometimes indicate spurious fitness because of nervous vagaries.[10] Performance tests are inextricably involved with the nervous system. Emotion can ruin a race or a functional test. In fact, athletes in condition can "pull" muscles, which is about the ultimate in failure of function.

The depth of breathing determines the flarimeter tolerances directly. A distance runner gave an average increase in tolerance of 34 seconds, after 3 minutes of persistent moderate overbreathing. In spite of this marked effect, however, it is better not to allow the men to become too respiration-conscious, for it is emotionally upsetting. If the maximum length of blow (T_m) must be used because the systolic response cannot be, it is advisable to standardize on just one minute of the deepest possible overbreathing. Then the longest possible blow becomes frankly a prowess test, and its length can be called T_{ma} (the subscript, a, for "acapnic"). There is a large factor of performance in T_{ma}, but it should be at least 20 seconds longer than T_m. Twenty-nine tests on seventeen athletes showed that one minute of maximum overbreathing increased flarimeter tolerances by more than one-third.

The overbreathing washes CO_2 out of the blood, thus changing the acid-base balance, but such changes can be produced also by eating acid salts such as NH_4Cl, as in the experiments of Haldane. These produce direct changes in the buffer action of the blood. Drugs, however, produce their effect through the nervous system. Thus, if alcohol is taken in sufficient quantitites it can drug the respiratory center and so make the flarimeter responses sluggish. This was

encountered one morning at the end of a season in a member of the crew who had celebrated his roommate's twenty-first anniversary the night before, and whose T_0 was 64 instead of its usual value of 13. He was surprised to find the blows easier to hold than ever, indeed he blew 84 seconds without reaching T_{20}. He confessed to an awful headache. The same effect was observed in varying degrees in other athletes when they broke training, but the best example is given in Table VIII.

TABLE VIII. EFFECT OF ALCOHOL (ON T24)

	MEDIANS AT PEAK TRAINING (7 TESTS)	OUT OF TRAINING (HANGOVER STAGE)			
		5-21-40		6-2-40	
At Rest—Sitting					
R	60	64	64	84	80
S	126	128	128	108	118
D	88	92	94	88	96
P	40	36	34	20	22
F	23	23	22	17	18
After Std. Stimulus					
S_1-S	18		18		19
D_1-D	0		0		6
R′	48		52		80
S_2-S	10		8		13
F′	27		27		28
Flarimeter Tolerances					
T_0	15	21	20	47	42
T_{20}	35	60	48	65	58
T_{30}	44	65	57	68	59
Av. T	32	49	42	60	53

This man (T24) was a good distance runner and at his peak about November 6, 1939. The next spring he was tested twice in the "hangover" stage. The first time was at 5 P.M. on a Tuesday (May 21, 1940). His companion said that T24 had imbibed about a dozen cans of beer and five or six Scotch and sodas on Saturday night, and repeated this on both Sunday and Monday.

He was unsteady in the step exercise but remarked without prompting that the 30-second blow was easier than ever. Being a premedical student he was interested in the effect, and volunteered for the "morning after next time." The test on June 2, 1940 was made at 10 A.M. on a Sunday morning, just after waking him up. (Notice the reduced blood flow index F.) He could not remember how he got home but thought he had "about 18 beers and 2 Scotch." He agreed that his previous test was after more alcohol, but spread over 3 days, with at least 15 hours to recover. This time the recovery period was only 5 hours. From these two examinations it is evident that alcohol can easily increase the average flarimeter tolerance (T) by 20 seconds or more. The narcotic effect of other drugs should be similar.

At some stages of intoxication and recovery the opposite effect of increased irritability is observed. For example, two days after a victory dinner some of the athletes show a reduction in T but most show little residual effect. The day after a celebration the reduction in T seldom reaches 10 seconds. The irritability is probably chiefly nervous, and may not be essentially different from the hyper-reaction which characterizes the early stages of many circulatory impairments. The exaggerated effect of minor sources of irritation upon the nervous system, however, advises caution in any quantitative interpretation of functional tests of the circulation.

The most characteristic feature of athletic training is the stability produced in the circulatory responses. There is a steady cumulative effect of training, but this is small, and most of it has already been acquired before reaching college. A good example is given by the results of an intercollegiate champion swimmer, summarized in Table IX.

TABLE IX. EFFECT OF TRAINING ON INTERCOLLEGIATE CHAMPION SWIMMER (S30): TESTS AT PEAK, SUCCESSIVE YEARS

DATE OF TEST	3-3-41	3-12-42	3-3-43
Sitting at Rest			
R	68	64	58
S	124	116	126
D	82	84	88
P	40	32	38
F	27	20	22
Responses to Standard Stimulus			
S_1-S	30	18	18
D_1-D	0	8	0
R′	60	64	52
S_2-S	8	—8	—6
D_2-D	2	2	—4
F′	35	20	24
Flarimeter Tolerances			
T_0	15	15	20
T_{20}	44	47	48
T_{30}	49	50	58
Av. T	36	38	42

Extreme flarimeter tolerances, such as those of S1, the second swimmer in Table V, are probably due to excessive practice in holding the breath. Pearl divers are known to develop extreme breath-holding ability. After following S1 for more than three years he suggested during the final test that as a boy he got the idea that a champion must be able to swim long distances under water, and so he developed this ability by long practice. Moreover, he never stopped training. This, apparently, conditioned his respiratory center to tolerate CO_2 much beyond the usual level.

Most of the athletes have longer tolerances when out of training. At the peak of condition their optimum T's become shorter, as if tuned up to concert pitch. There are so many disturbing factors when training is broken, however, which influence the tolerances in opposite directions, that in practice the tests must be interpreted clinically.

Ordinary normal individuals cannot be expected to yield stable results. They must and do reflect the irregular conditions of everyday life. In such situations the most significant signs are the hyper-reactions, the excessive responses to standard stimulus, and abnormally decreased flarimeter tolerances. They warrant further study, for the literature abounds in evidence that many such conditions are merely emotional, without serious consequence. Sluggish responses are not usually of so much value, except for comparison with previous tests on the same individual. To be sure, some advanced cases are sluggish, but invalids make poor subjects for performance tests.

It is evident that flarimeter tolerances, like blood pressures and heart rate, are resultant effects and that just what is producing the changes in them cannot be decided from flarimeter tests alone. However, by comparing all values of a retest with those of previous tests made under precisely comparable conditions, a stable present condition is indicated with some reliability. Such results are most reassuring to an athlete who lacks self-confidence.

SUMMARY

A standard flarimeter technique is presented for tests on athletes. A blow of fixed length (30 seconds) is begun 10 seconds after Master's standard two-step exercise. Responses to this standard stimulus are reproducible.

Normal standards are established for college male athletes. The factors influencing the results are studied in some detail, to provide a background for the interpretation of the tests. Emotion is the most important. Indeed, functional tests, like athletic performance, seem to be essentially tests of nerve coordination.

I wish to thank the Princeton University Department of Health and Physical Education for their courtesy and help at every stage, the men who graciously volunteered for these tests, and the coaches, especially Howie Stepp and Matty Geis, for their cooperation.

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THE PORTAL VENOUS PRESSURE IN ORGANIC HEART DISEASE

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INTRODUCTION

THE hepatic veins were first catheterized by Warren and Brannon[8] in 1944. They succeeded without incident in passing a catheter into the hepatic veins of six normal individuals and thereby estimated the oxygen, sugar, and non-protein nitrogen content of the blood from the hepatic veins and compared the levels with those found in the arterial blood. In the following year Bradley and associates[1] calculated the hepatic blood flow in twenty-three normal patients, and in 1947, Myers[5] showed that in normal individuals the hepatic blood flow was twenty per cent of the cardiac output and that the splanchnic oxygen consumption was twenty-five per cent of the total oxygen consumption. In 1948, Myers carried out these investigations in thirteen patients with varying degrees of congestive cardiac failure and compared the results with those in a series of normal adults. The findings showed that in congestive cardiac failure the hepatic blood flow was reduced and that this reduction was in proportion to the lowered cardiac output. The fall in the hepatic blood flow was compensated by an increase in the arterial hepatic venous oxygen difference, thereby providing a normal splanchnic oxygen consumption. Friedman and Weiner[2] in 1951 estimated simultaneous occlusive hepatic venule pressures and portal venous pressures in dogs, and in the same year a similar experiment in cats was made by Myers.[6] Both teams of investigators found that the two pressures were comparable and agreed closely. Myers then extended this experiment to man and proved conclusively that the portal venous pressure could be measured by catheterization of the hepatic veins. He passed one catheter into the hepatic vein via the right auricle and inferior vena cava, and another directly into the portal vein. The average mean readings were 4.8 mm. Hg and 3.3 mm. Hg, respectively, in these normal patients. The investigation was then made on seven patients with portal hypertension secondary to Laennec's cirrhosis; the mean pressure in these cases was the same for both the portal and the occlusive hepatic venule pressure, being 20.1 mm. Hg. This means of measuring the portal venous pressure is comparable with the estimation of the left auricular pressure by occlusive catheterization of the pulmonary capillaries. Since Myers has published his results Milnes Walker[4] has estimated the pressure in the portal vein by direct catheterization in twenty normal patients. His results for the

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portal venous pressure range from 6 to 11 mm. Hg. He also measured the pressure in three patients with known portal hypertension; the mean pressure result was 13 mm. Hg. Gray[3] has also measured the direct portal venous pressure and gives 15 mm. Hg as the upper limit of normal for the portal venous pressure.

PRESENT INVESTIGATION

During the course of a clinical and laboratory survey of liver function on fifty-seven cases of congestive cardiac failure, hepatic catheterization was carried out in four cases with gross liver enlargement. It was only attempted if it caused no distress, and the number of cases chosen was correspondingly limited. Thirteen patients who had organic heart disease and who had never been in failure were also catheterized and served as a control. In all these cases it was possible to catheterize the hepatic veins through the right side of the heart. This was done by passing a catheter into the right auricle and advancing it along the inferior vena cava, and thence into the hepatic vein, the right branch of which was entered in every case. With the catheter lying free in the hepatic vein a pressure was recorded, and this was labeled the hepatic venous pressure (H.V.P.), the result was calculated in mm. Hg above the sternal angle. After recording this pressure, the catheter was pushed along the hepatic vein, passing deep into the liver, and when it was no longer possible for it to advance any further, that is, when it was wedged in the hepatic vein, a pressure reading was recorded; this was called the occlusive hepatic venule pressure (O.H.V.P.). To confirm these readings, in every case the fluid level in the manometer was raised and the pressure in the column of fluid allowed to fall. The new readings were checked against the previous ones and in each instance they agreed. The catheter was then withdrawn and the whole procedure repeated. X-rays were taken of the catheter lying free in and occluding the hepatic vein in all the cases. It may be that the catheter never blocked the hepatic veins, but we are not inclined to this view. If we accept Myers' theory that the occlusive hepatic venule pressure is equivalent to the portal venous pressure, then this technique served as a means of assessing the degree of portal hypertension.

TABLE I

		READINGS IN MM. HG FROM THE STERNAL ANGLE			
		R.A.	I.V.C.	O.H.V.P.	H.V.P.
Control	Range	1 – 10	0 – 5	1 – 6	– 5 – 6
	Mean	1.9	1.2	3.3	1.2
Liver +	Range	1.5 – 12		7.5 – 12	3.5 – 12
	Mean	8	9	10	9

RESULTS

The results would seem to show that the catheter must have occluded the hepatic vein, as the pressure was slightly higher than that in the unblocked hepatic vein in thirteen of the seventeen cases and in the other four the two readings were the same (Table II).

The readings that were obtained for the occlusive hepatic venule pressure range from 1 to 12 mm. Hg. The highest reading in the control cases was 6 mm. Hg, whereas in the four cases in which there was cardiac failure with liver enlargement, the lowest reading was 7.5 mm. Hg and the highest 12.5 mm. Hg (Table I).

TABLE II

NO.	PATIENT	SEX	AGE	PRESSURE IN MM. HG FROM THE STERNAL ANGLE			
				R.A.	I.V.C.	O.H.V.P.	H.V.P.
1	O.S.	F	32	1	1	4	1
2	M.H.	F	31	−1	0	1	−1
3	E.R.	F	36	−1	0	5	3
4	J.L.	F	30	1	—	2	1
5	D.R.	M	32	1.5	0	2	1
6	D.C.	F	14	1.4	3.5	3	1.4
7	A.R.	F	28	−1	−1	1	0
8	M.G.	F	30	1.5	—	5	1.5
9	E.H.	F	33	3.5	3	3.5	3.5
10	N.W.	F	42	5	5	6	6
11	E.B.	F	36	1	—	2	1
12	B.F.	F	32	−1	1	4	1
13	N.A.	F	23	2	2	3	2
14	B.T.	F	32	10	9	12	11
15	E.D.	F	38	12	—	12	12
16	I.G.	F	13	1.5	—	7.5	3.5
17	C.M.	F	42	7.5	—	7.5	7.5

It can be seen from the results in Table II that when the hepatic venous pressure was raised there was an associated high right auricular pressure, which appears to indicate that the high hepatic venous pressure was due to a direct back pressure, and was in no way related to portal hypertension (Cases 10, 14, 15 and 17, Table II). Case 16 was that of a young girl with valvular disease of the heart and liver enlargement which had been present for more than a year without any other signs of failure. This combination of physical signs is seen quite often in children. From our results it will be seen that her right auricular pressure was normal, that the hepatic venous pressure was slightly raised, and that the occlusive hepatic venule pressure was even higher. It is possible that some other factor than direct back pressure can be responsible for the hepatomegaly in such a case, but it is impossible to draw any conclusions from one case. From our findings, none of the cases had portal hypertension as defined by Myers, and in the four cases with failure the changes in the liver would appear to be due to venous congestion secondary to a direct back pressure from the right side of the heart.

SUMMARY

Catheterization of the hepatic veins was performed in four cases of congestive cardiac failure and in thirteen patients with compensated organic heart disease in an attempt to evaluate the portal venous pressure. Portal hypertension was not present in any of the cases and the results would appear to show that the raised readings were due solely to congestive failure.

I am grateful to Dr. E. Noble Chamberlain for allowing me to catheterize his patients, and for his clinical guidance and helpful criticism.

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Announcement

The eighth annual meeting of the WESTERN SOCIETY FOR CLINICAL RESEARCH will be held Jan. 28 and 29, 1955, at Carmel, Calif.

Information regarding the meeting may be obtained from Herbert N. Hultgren, M.D., Secretary-Treasurer, Stanford Hospital, San Francisco 15, Calif.

THE CONTROL OF CERTAIN CARDIAC ARRHYTHMIAS WITH ISOPROPYLNOREPINEPHRINE

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FOR many years sympathomimetic substances have been studied in an attempt to establish their role in the management of cardiovascular disorders. Recently a new member, isopropylnorepinephrine (I.P.N., Isuprel) has joined the group and is now being subjected to intensive evaluation. I.P.N. differs from the parent compound, epinephrine, in that an isopropyl group has been substituted for the methyl group in the chemical structure. The new amine has been found to possess many pharmacologic similarities as well as important differences from epinephrine.

Like epinephrine, I.P.N. causes a marked increase in cardiac rate and in the amplitude of myocardial contractions although quantitatively it is more active in both respects.[1-4] It increases stroke volume,[3] raises coronary artery flow secondary to the increased heart rate,[5] and shows a definite inotropic effect on heart muscle.[6] Both epinephrine and I.P.N. have been reported to produce transient electrocardiographic T-wave inversion.[3]

Although both materials augment myocardial irritability, I.P.N. has been noted to increase the irritability more than any other sympathomimetic compound studied.[7] It has also shown the least tendency to produce cardiac automaticity.[7] In this respect, the injection of epinephrine or norepinephrine into cats anesthetized by the intratracheal administration of a hydrocarbon produced ventricular fibrillation while no arrhythmia was observed with the use of I.P.N. under similar circumstances.[8] Opinions regarding blood pressure changes from administration of I.P.N. have varied somewhat, although generally there has been reported a slight rise in systolic and a fall in diastolic pressures.[9,10] I.P.N., unlike epinephrine, has not been observed to cause tremor, blanching of the skin, or an increase in blood sugar.

The Morgagni-Stokes-Adams syndrome is known to result from ventricular asystole, ventricular tachycardia, and ventricular fibrillation.[11-13] In view of these latter mechanisms, it had been hoped that quinidine and procaine amide might be of value in therapy. Unfortunately it was discovered that the administration of these drugs to people with complete heart block resulted in prefibrillatory mechanisms or in ventricular fibrillation.[12,14,15] Quinidine was assumed to produce irregular variations in the refractory periods of different

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areas of the myocardium and so allow the development of the ventricular fibrillation.[12] Epinephrine, the former drug of choice for patients with ventricular asystole, has now been postulated to be dangerous when ventricular tachycardia or ventricular fibrillation is the basic cause of the syncope. Its ability to produce ventricular fibrillation in patients with ventricular premature systoles and ventricular tachycardia would indicate that the substance might increase the frequency and severity of the seizures.

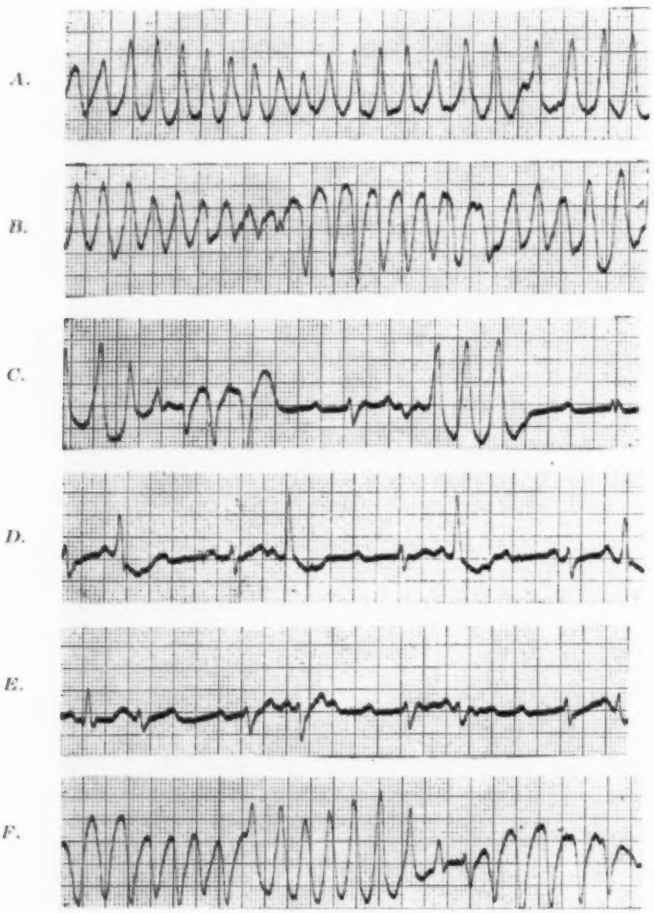

Fig. 1.—Lead I. *A*, Before I.P.N. *B*, 15 minutes after intravenous Pronestyl. 8 mg. of I.P.N. given subcutaneously in divided doses. *C*, 5 minutes after I.P.N. *D*, 15 minutes after I.P.N. *E*, 20 minutes after I.P.N. *F*, 30 minutes after I.P.N.

The purpose of this paper is to present the results of the administration of I.P.N. to patients with several types of cardiac arrhythmias. Included in the examples are the records of patients who experience Stokes-Adams seizures on the basis of ventricular tachycardia.

EXAMPLES

In Fig. 1 are shown the electrocardiograms of a patient with complete heart block who had Stokes-Adams seizures with ventricular tachycardia. The electrocardiograms demonstrate the ineffectiveness of 800 mg. of intravenous procaine amide on the ventricular tachycardia, serving only to increase the number of pacemakers present. Subcutaneously injected I.P.N. in contradistinction caused abrupt cessation of the tachycardia. Although not shown, the same result was obtained in this case with intravenous I.P.N. on several occasions. I.P.N. when administered to a second patient with a similar arrhythmia resulted in the abolition of multiple ventricular foci

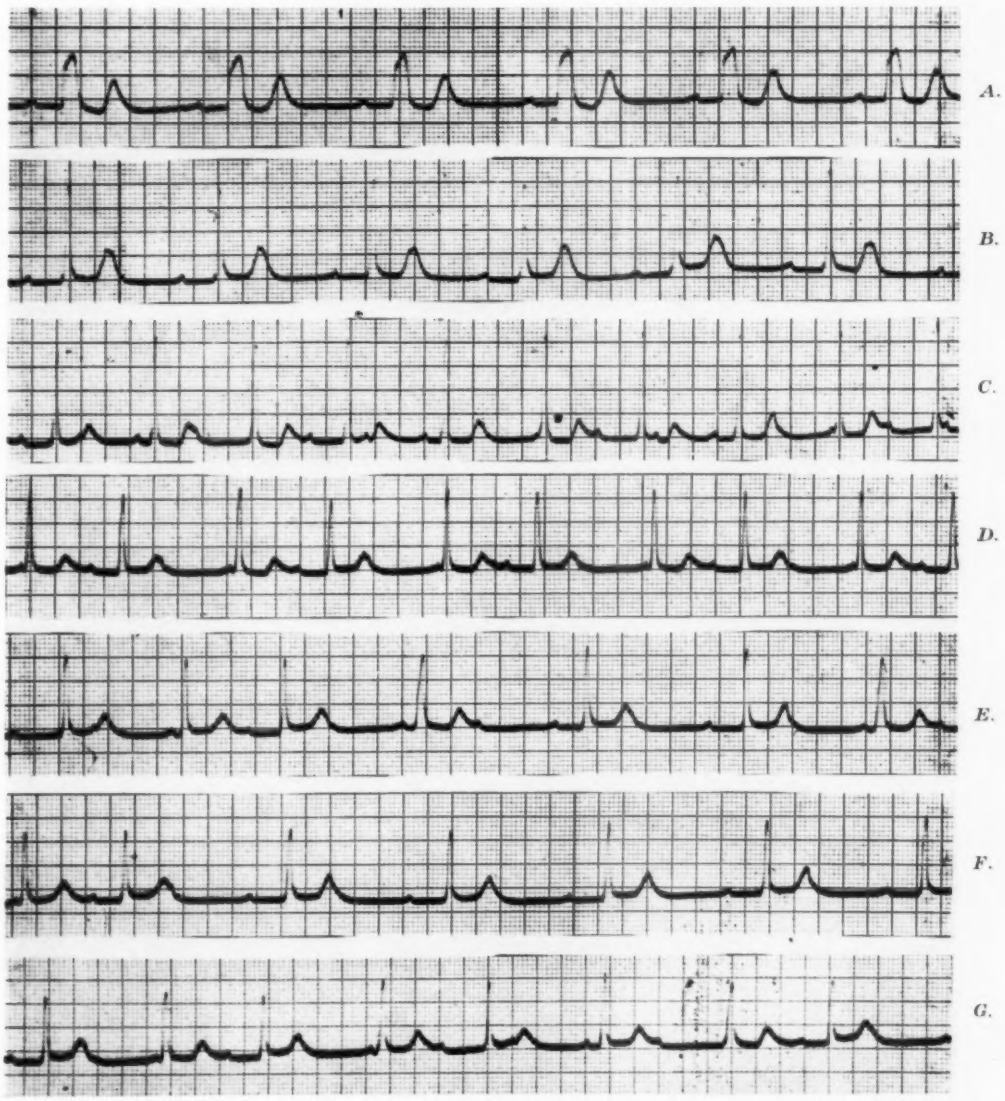

Fig. 2.—*A*, Lead I at the time of administration of 0.2 mg. I.P.N. *B*, 1 minute after I.P.N. *C*, 8 minutes after I.P.N. *D*, 48 minutes after I.P.N. *E*, 1 hour and 8 minutes after I.P.N. *F*, 1 hour and 18 minutes after I.P.N. *G*, 2 hours and 18 minutes after I.P.N.

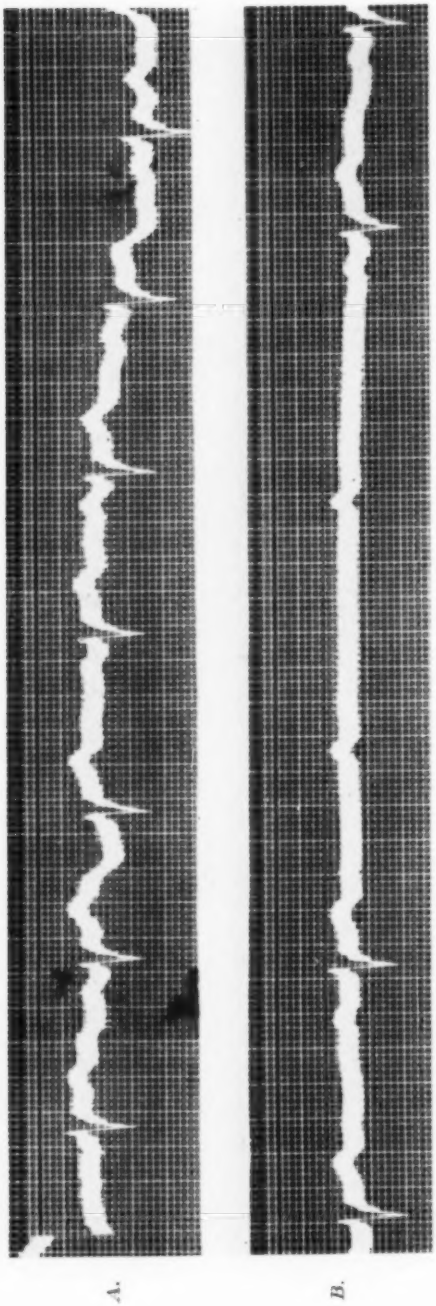

Fig. 3.—Lead II. *A*, Before carotid sinus pressure. *B*, With right carotid sinus pressure.

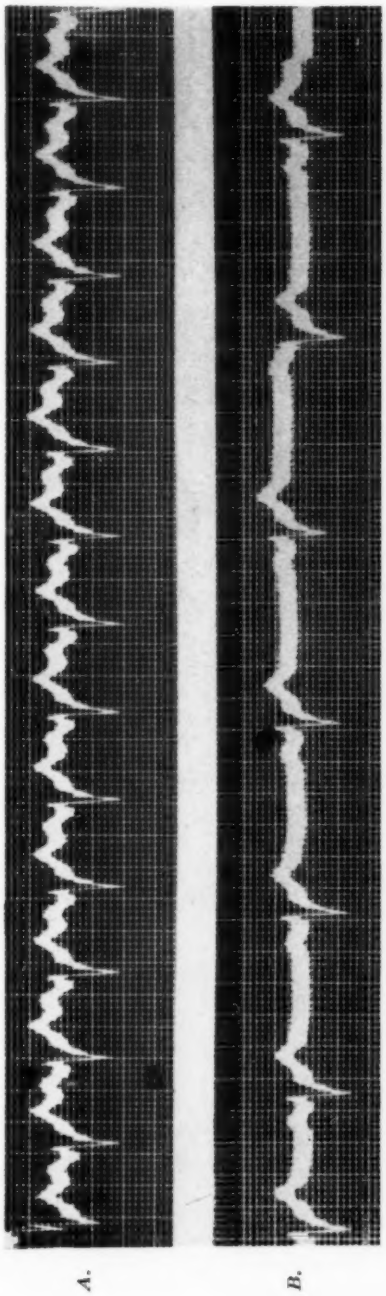

Fig. 4.—Lead II. *A*, After 0.2 mg. of I.P.N. and before right carotid sinus pressure. *B*, After 0.2 mg. of I.P.N. and with right carotid sinus pressure.

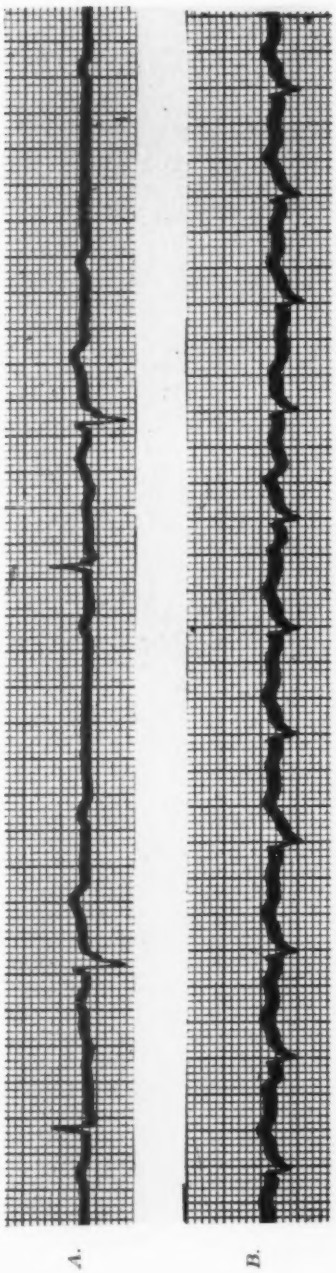

Fig. 5.—Lead II. *A*, After atropine and ephedrine. *B*, After 0.2 mg. of I.P.N.

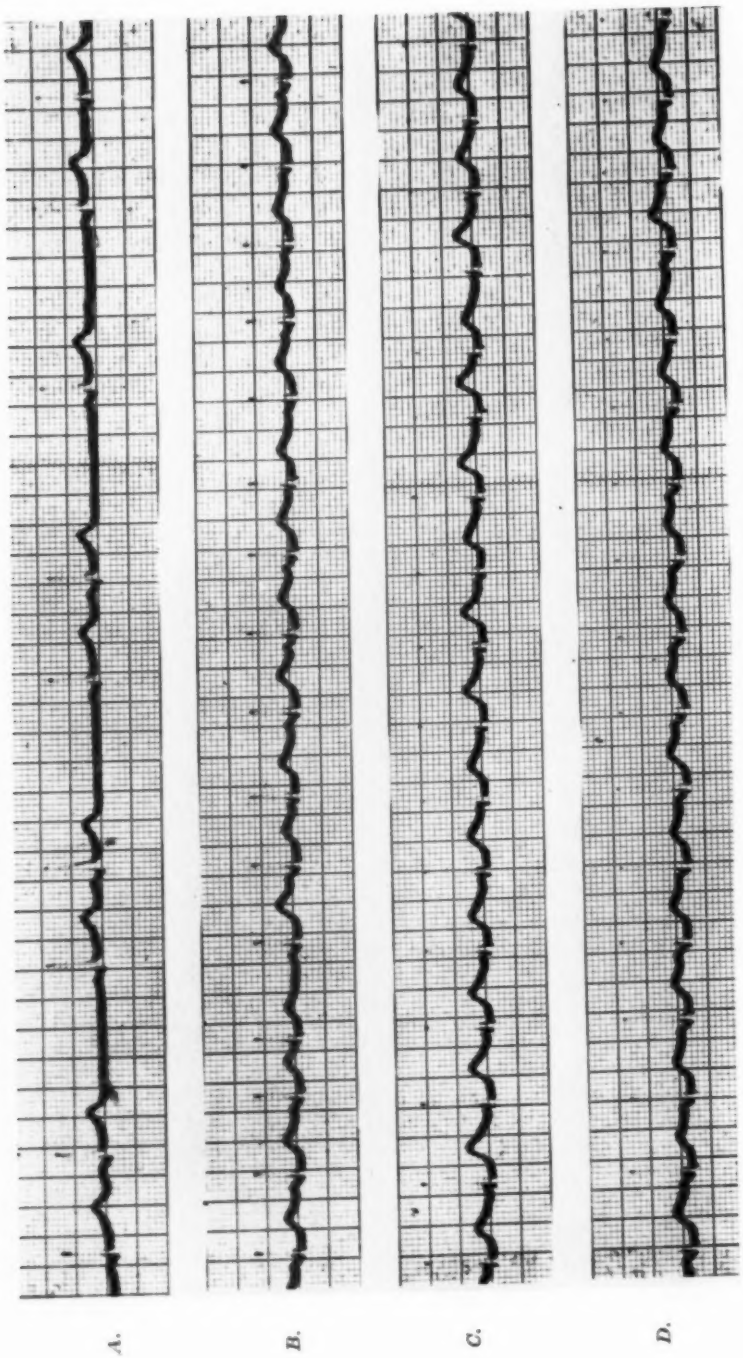

Fig. 6.—*A*, Lead I at the time of administration of 0.2 mg. of I.P.N. subcutaneously. *B*, Lead II, 10 minutes after I.P.N. *C*, Lead II, 17 minutes after I.P.N. *D*, Lead II, 32 minutes after I.P.N.

and the establishment of a single pacemaker in an area near the auriculoventricular node. The change in ventricular rate prevented the hourly recurrence of syncope. She was placed on sublingual I.P.N. (20 mg. every four to six hours) as maintenance therapy and now has been free of syncopal spells for several months. Previously she had been uncontrolled on ephedrine and Banthine.

The electrocardiograms demonstrated in Fig. 2 are those of a patient with complete auriculoventricular block, but without ventricular tachycardia or fibrillation. The patient was a man who was admitted with his fourth myocardial infarction. At the time of recording of Fig. 2 he was comatose, regaining consciousness only for short periods during which he complained of severe substernal pain. Electrocardiograms taken several hours prior to Fig. 2,*A* showed complete A-V block and it is our belief that Fig. 2,*A* also represents this phenomenon with every second P wave hidden in the ventricular T waves. As further evidence it was also found that the P-R interval became progressively shorter over a period of recording. Within one minute after I.P.N. subcutaneously the ventricular complexes had changed markedly with an increase in rate apparent. A new pacemaker had also been established, probably high in the Bundle of His near the auriculoventricular node. The auricular rate was similarly increased. The ventricular rate continued to increase in Fig. 2,*C* and the complete auriculoventricular block again became obvious. The rhythm in Fig. 2,*D* would seem to represent sequences of sinus beats, dropped beats, and auriculoventricular nodal escape complexes. Symptomatically the result was dramatic. The patient became progressively alert as his ventricular rate increased and within fifteen minutes after his initial injection his angina had also disappeared. After I.P.N. sublingually, the rate and characteristics of the complexes continued as with the parenteral administration and within 72 hours, on maintenance I.P.N., the patient returned to a sinus mechanism. Three other patients with complete heart block were also treated with I.P.N. under similar circumstances and demonstrated results very comparable to the example just described. One patient was observed, however, who showed an increase in his ventricular rate but also experienced the temporary establishment of a pacemaker lower in the conduction system.

Figs. 3, 4, and 5 show typical responses to I.P.N. in patients with hyperactive carotid sinuses. Fig. 5 demonstrates the electrocardiogram of an elderly man who at this time was experiencing spells of syncope occurring nearly every two to three minutes. He had not been relieved by atropine and ephedrine but developed a sinus rhythm and cessation of syncope immediately after subcutaneous I.P.N. In our experience with other patients with the hyperactive carotid sinus syndrome, it was noted that the development of escape beats from several areas was not unusual. These beats were usually of auriculoventricular nodal origin.

The electrocardiogram in Fig. 6 was taken from a man who had had a recent cerebral thrombosis but had no obvious cardiac problem other than an arrhythmia. After I.P.N. his rhythm became regular and more rapid, although the pacemaker shifted from the auriculoventricular node area in Fig. 6,*C* to a sinus origin in Fig. 6,*D*. There was no recurrence of his arrhythmia.

COMMENT

In our series of 28 patients treated with I.P.N. certain consistent results have been observed. There has generally been a rise of 10 to 20 mm. Hg in the systolic blood pressure and a similar drop in diastolic pressure. In cases of complete auriculoventricular block the rate of the pacemaker has always increased considerably and has, with one exception, relocated in the vicinity of the auriculoventricular node. When dissociation persists both the auricular and ventricular rates have increased simultaneously although not always to the same degree. In cases without complete heart block I.P.N. exerted its primary effect upon the sinus area although a definite action on the auriculoventricular node was also observed. In no case was ventricular fibrillation or ventricular tachycardia induced by I.P.N. although the latter was abruptly halted in two patients.

Some depression of the S-T junction was noted in Cases 5 and 6 as has been reported by others.[10] The etiology of this change has not been definitely established. No definite changes were noted in the T waves.

Several patients developed palpitation with 0.2 mg. of I.P.N. subcutaneously, but no patient experienced the feelings of air hunger or substernal oppression reported by others.

SUMMARY AND CONCLUSIONS

The action of I.P.N. on several types of cardiac arrhythmia has been described. The use of I.P.N. in patients having ventricular tachycardia in connection with the Morgagni-Stokes-Adams syndrome is reported. One of these patients, as well as those with hyperactive carotid sinus syndromes, has been maintained on sublingual I.P.N. for periods of three or four months with good results. I.P.N. would now appear to be the drug of choice in these conditions.

The I.P.N. used in these cases was graciously donated by Winthrop-Stearns, Inc., Buffalo, N. Y.

We would like to express our gratitude to Dr. E. H. Drake for his help in this work. Also to Drs. F. J. Smith, J. T. Howell, and R. F. Ziegler for reviewing this paper.

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INDEX TO VOLUME 48

AUTHORS INDEX

A

ADLERSBERG, DAVID. (*See* Boas, Elster, and Adlersberg), 485

AYALA Y DE LANDERO, CARLOS. A mathematical method to determine the magnitude of electrical axis, 894

B

BACKBIER, F. G. (*See* Burger, Tolhoek, and Backbier), 249

BAKER, CHARLES R. (*See* Sobin, Carson, Johnson, and Baker), 416

BATTERMAN, ROBERT C. The comparative diuretic effectiveness of mercumatilin and meralluride with and without concomitant administration of ammonium chloride, 780

BEAMISH, R. E., PERRY, W. F., AND STORRIE, V. MARIE. Observations on thyroid function in hypertensive patients treated with potassium thiocyanate, 433

BEATTY, DAVID C. (*See* Yu, Lovejoy, Joos, Nye, and Beatty), 544

BERGLUND, ERIK. (*See* Isaacs, Berglund, and Sarnoff), 66

BERNSTEIN, LIONEL M., PASCALE, LUKE R., SCHOOLMAN, HAROLD M., AND FOLEY, EDMUND F. Intravenous procaine amide as an aid to differentiate auricular flutter with bundle branch block from paroxysmal ventricular tachycarda, 82

——. (*See* Pascale, Bernstein, Schoolman, and Foley), 110

BJÖRK, VIKING OLOV, BLAKEMORE, WILLIAM S., AND MALMSTRÖM, GUNNAR. Left ventricular pressure measurement in man, 197

——, MALMSTRÖM, GUNNAR, AND UGGLA, LARS-GUSTAF. Comparison of the oxygen tension in blood from the left atrium and a systemic artery, 8

BLACK, MARTIN M., AND LYONS, RICHARD H. Prolonged depression of atrioventricular conduction caused by large dosages of protoveratrine, 266

BLAKEMORE, WILLIAM S. (*See* Björk, Blakemore, and Malmström), 197

BLICKMAN, J. R. (*See* Durrer, van der Tweel, and Blickman), 13

BLOUNT, S. GILBERT, JR. (*See* Denst, Edwards, Neubuerger, and Blount), 506

——. (*See* McCord, Swan, and Blount, Jr.), 405

BLUMENFELD, SERGE. (*See* Scherf, Blumenfeld, Golbey, Ladopoulos, and Roth), 573

BOAS, ERNST P., ELSTER, SAMUEL K., AND ADLERSBERG, DAVID. Calcific aortic stenosis: study of serum cholesterol, 485

BOHL, ROBERT W. (*See* Goulder, Kissane, and Bohl), 906

BORDUAS, JEAN LOUIS. (*See* Rakita, Borduas, Rothman, and Prinzmetal), 351

BRANDFONBRENER, MARTIN, AND EISENBERG, HENRY. The aortic electrokymogram in normal subjects and patients with syphilitic aortic insufficiency, 54

BRAUNSTEIN, JOHN. (*See* Simon, Iglauer, and Braunstein), 185

BRIGGS, GORDON W., CARLSON, HAROLD A., AND HOUSEWORTH, JOHN H. Superior vena cava obstruction with complete obstruction of the right main pulmonary artery, 288

BRODY, DANIEL A., MCKAY, B. P., AND ROMANS, WILLIAM E. The axostat, 589

——. (*See* Little, Brody, and Tacket), 721

——. The meaning of lead vectors and the Burger triangle, 730

BROTMACHER, LEON. The association of the Wenckebach phenomenon with auricular flutter, 629

BROWN, ALBERT F. (*See* Sprengel and Brown), 796

BUCHT, HÄRJE. (*See* Ek, Bucht, and Werkö), 102

BURACK, BERNARD. (*See* Grossman, Kantrowitz, Burack, and Haimovici), 471

BURCH, G. E., AND RAY, C. T. Mechanism of the hepatojugular reflux test in congestive heart failure, 373

BURGER, H. C., TOLHOEK, H. A., BACKBIER, F. G. The potential distribution on the body surface caused by a heart vector, 249

C

CABAUD, PHILIP G. (*See* Dorney and Cabaud), 459

CARLSON, HAROLD A. (*See* Briggs, Carlson, and Houseworth), 288

CARR, HENRY A. (*See* Stewart and Carr), 293

CARSON, MERL J. (*See* Sobin, Carson, Johnson, and Baker), 416

CHESTERMAN, JUDSON T., AND WHITAKER, WILLIAM. Mitral and tricuspid valvotomy for mitral and tricuspid stenosis, 631

COHEN, NATHANIEL. (*See* Douglas and Cohen), 340

COHEN, SAMUEL L. (*See* Levin and Cohen), 637

COLBECK, J. C., AND SHAW, J. M. Coronary aneurysm with arteriovenous fistula, 270

CRAIG, ROBERT L., AND LEARNED, BERYLE B. Patterns of the anterior descending branch of the left coronary artery in the dog, 455
CRUMPTON, CHARLES W. (*See* Tuchman, Sletten, and Crumpton), 449
CUBBERLY, ROBERT. (*See* Fowler, Cubberly, and Dorney), 1

D

DEMPSEY, MARY E. (*See* Wilson, Hoseth, Sadoff, and Dempsey), 671
DENST, JOHN, EDWARDS, ALFRED, NEUBUERGER, KARL T., AND BLOUNT, S. GILBERT, JR. Biopsies of the lung and atrial appendages in mitral stenosis: correlation of data from cardiac catheterization with pulmonary vascular lesions, 506
DICKES, ROBERT. (*See* Edson, Flamm, Dickes, Tobin, and Loeb), 897
DONOSO, EFRAIM. (*See* Kuhn, Donoso, and Sapin), 280
DONTAS, A. S. (*See* VanderKolk, Dontas, and Hoobler), 95
DORNEY, EDWARD. (*See* Fowler, Cubberly, and Dorney), 1
DORNEY, EDWARD R., AND CABAUD, PHILIP G. Massive left atrial thrombosis and recurring pleural effusion, 459
——. (*See* Fowler and Dorney), 36
DOUGLAS, ALBERT H., AND COHEN, NATHANIEL. The vector and algebraic relationship of the CF and V chest leads, 340
DURRER, D., VAN DER TWEEL, L. H., AND BLICKMAN, J. R. Spread of activation in the left ventricular wall of the dog. III, 13

E

EDEIKEN, JOSEPH. Elevation of the RS-T segment, apparent or real, in the right precordial leads as a probable normal variant, 331
EDSON, JOHN N., FLAMM, GERALD H., DICKES, ROBERT, TOBIN, MICHAEL, AND LOEB, LAURENCE. Thoracic ballistocardiography, 897
EDWARDS, ALFRED. (*See* Denst, Edwards, Neubuerger, and Blount), 506
EISENBERG, HENRY. (*See* Brandfonbrener and Eisenberg), 54
EK, JAN, BUCHT, HÄRJE, AND WERKÖ, LARS. The influence of a rapid infusion of glucose on renal dynamics and sodium excretion in patients with arterial hypertension, 102
ELLIS, RICHARD M. (*See* Rushmer, Tidwell, and Ellis), 835
ELSTER, SAMUEL K. (*See* Boas, Elster, and Adlersberg), 485
EPSTEIN, FREDERICK H. (*See* Hyman and Epstein), 540

F

FLAMM, GERALD. (*See* Edson, Flamm, Dickes, Tobin, and Loeb), 897
FOLEY, EDMUND F. (*See* Bernstein, Pascale, Schoolman, and Foley), 82
——. (*See* Pascale, Bernstein, Schoolman, and Foley), 110
FORD, RALPH V., LIVESAY, W. R., SPURR, CHARLES, AND MOYER, JOHN H. Treatment of hypertensive emergencies: use of Veriloid-in-Oil intramuscularly, 123
FOWLER, NOBLE O., AND DORNEY, EDWARD R. Studies of the P loop of the spatial vectorcardiogram: the normal P loop, 36
——, CUBBERLY, ROBERT, AND DORNEY, EDWARD. Pulmonary blood distribution and oxygen diffusion in mitral stenosis, 1
FOX, HENRY M., RIZZO, NICHOLAS D., AND GIFFORD, SANFORD. Psychological observations of patients undergoing mitral surgery, 645
FRANK, ERNEST. An equivalent circuit for the human heart-body electrical system, 738
FRIEND, DALE G., O'HARE, JAMES P., AND LEVINE, HAROLD D. Action of triethanolamine trinitrate in angina pectoris, 775
FUMAGALLI, BRUNO. Unipolar value of standard limb leads: Lead −VR and rational arrangement of limb leads, 204

G

GAMNA, GIORGIO. (*See* Luisada and Gamna), 826
GECKELER, GEORGE D., LIKOFF, WILLIAM, MASON, DANIEL, RIESZ, R. R., AND WIRTH, CHARLES H. Cardiospectrograms, 189
GIFFORD, SANFORD. (*See* Fox, Rizzo, and Gifford), 645
GOETZ, A. A., AND GROPPER, A. N. Perforation of the interventricular septum, 130
GOLBEY, MAURICE. (*See* Scherf, Blumenfeld, Golbey, Ladopoulos, and Roth), 573
GOODALE, WALTER T. (*See* Rudolph, Nadas, and Goodale), 808
GOULDER, NORMAN E., KISSANE, R. W., AND BOHL, ROBERT W. Provocative aspects of lipotropic therapy in angina pectoris, 906
GROPPER, A. N. (*See* Goetz and Gropper), 130
GROSS, DESIDERIO. Quantitative estimation of ventricular strain in the limb leads, 881
GROSSMAN, JACOB, KANTROWITZ, ADRIAN, BURACK, BERNARD, AND HAIMOVICI, HENRY. Mitral commissurotomy followed by late arterial embolism, 471

H

HAIMOVICI, HENRY (*See* Grossman, Kantrowitz, Burack, and Haimovici), 471
HALLINGER, LEONARD N. (*See* Schwartz and Hallinger), 390

HANDLEY, CARROLL A. (*See* Moyer and Handley), 173
HEFFER, E. T. (*See* Kroop, Heffer, and Shackman), 612
HEFFER, ERNEST T. (*See* Shackman, Heffer, and Kroop), 599
HEJTMANCIK, MILTON R. (*See* Stembridge, Hejtmancik, and Herrmann), 163
HELM, ROBERT A. The direction of mean QRS and T vectors, 224
HERRMANN, GEORGE R. (*See* Stembridge, Hejtmancik, and Herrmann), 163
HOFFMAN, IRWIN. (*See* Schwarzschild, Hoffman, and Kissin), 235
HOOBLER, S. W. (*See* VanderKolk, Dontas, and Hoobler), 95
HOSETH, WAYNE. (*See* Wilson, Hoseth, Sadoff and Dempsey), 671
HOUSEWORTH, JOHN H. (*See* Briggs, Carlson, and Houseworth), 288
HOWELL, MILTON. (*See* London and Howell), 152
HUNZICKER, WARREN J. (*See* Mitchell, Sackett, Hunzicker, and Levine), 684
HYMAN, JULIAN B., AND EPSTEIN, FREDERICK H. A study of the correlation between roentgenographic and postmortem calcification of the aorta, 540

I

IGLAUER, ARNOLD. (*See* Simon, Iglauer, and Braunstein), 185
——. (*See* Simon, Iglauer, and Scott), 624
IPPOLITO, THOMAS L., BLIER, JULIUS S., AND FOX, THEODORE T. Massive T-wave inversion, 88
ISAACS, JAMES P., BERGLUND, ERIK, AND SARNOFF, STANLEY J. Ventricular function, 66

J

JOHNSON, JOHN L. (*See* Sobin, Carson, Johnson, and Baker), 416
JOOS, HOWARD A. (*See* Yu, Lovejoy, Joos, Nye, and Beatty), 544

K

KANTROWITZ, ADRIAN. (*See* Grossman, Kantrowitz, Burack, and Haimovici), 471
KEYS, ANCEL. (*See* Taylor, Maloney, and Keys), 864
KING, T. SUMMERFIELD. The sinuatrial node in the rat, 785
KISSANE, R. W. (*See* Goulder, Kissane, and Bohl), 906
KISSIN, MILTON. (*See* Schwarzschild, Hoffman, and Kissin), 235
KORST, DONALD R., AND WASSERBURGER, RICHARD H. Auricular flutter associated with complete heart block, 383
KRAPIN, DAVID. Cure of enterococcal endocarditis of prolonged duration, 792
KROOP, IRVING G., HEFFER, E. T., AND SHACKMAN, N. H. An evaluation of electrophoresis in rheumatic fever, 612
——. (*See* Shackman, Heffer, and Kroop), 599
KUHN, LESLIE A., DONOSO, EFRAIM, AND SAPIN, SAMUEL O. Auricular tachycardia with Wenckebach phenomenon occurring during the course of cardiac catheterization, 280
KYLLÖNEN, K. E. J. (*See* Peräsalo and Kyllönen), 465

L

LADOPOULOS, CONSTANTINE. (*See* Scherf, Blumenfeld, Golbey, Ladopoulos, and Roth), 573
LASSER, RICHARD P., AND LOEWE, LEO. Cardiac and pulmonary artery pressure pulses in experimental mitral stenosis, 801
LEARNED, BERYLE B. (*See* Craig and Learned), 455
LEVIN, EUGENE B., AND COHEN, SAMUEL L. Idiopathic myocardial hypertrophy simulating rheumatic heart disease, 637
LEVINE, HAROLD D. (*See* Friend, O'Hare, and Levine), 775
LEVINE, SAMUEL A. (*See* Mitchell, Sackett, Hunzicker, and Levine), 684
LIKOFF, WILLIAM. (*See* Geckeler, Likoff, Mason, Riesz and Wirth), 189
LITTLE, ROBERT C., BRODY, DANIEL A., AND TACKET, HALL S. The axostat, 721
LIU, S. F. (*See* Simon and Liu), 497
LIVESAY, W. R. (*See* Ford, Livesay, Spurr, and Moyer), 123
——. (*See* Moyer, Livesay, and Seibert), 817
LOEB, LAURENCE. (*See* Edson, Flamm, Dickes, Tobin and Loeb), 897
LOEWE, LEO. (*See* Lasser and Loewe), 801
LONDON, FRANK, AND HOWELL, MILTON. Atrial flutter: 1 to 1 conduction during treatment with quinidine and digitalis, 152
LOVEJOY, F. W., Jr. (*See* Yu, Lovejoy, Joos, Nye, and Beatty), 544
LUISADA, ALDO A., AND GAMNA, GIORGIO. Clinical calibration in phonocardiography, 826
LYONS, RICHARD H. (*See* Black and Lyons). 266

M

MCCORD, MALCOLM C., SWAN, HENRY, AND BLOUNT, S. GILBERT, JR. Tricuspid stenosis: clinical and physiologic evaluation, 405
MCKAY, B. P. (*See* Brody, McKay, and Romans), 589
MALMSTRÖM, GUNNAR. (*See* Björk, Blakemore, and Malmström), 197
——. (*See* Björk, Malmström, and Uggla), 8
MALONEY, WILLIAM F. (*See* Taylor, Maloney, and Keys), 864
MASON, DANIEL. (*See* Geckeler, Likoff, Mason, Riesz, and Wirth), 189
MATTINGLY, THOMAS W. (*See* Sayer, Moser, and Mattingly), 42

MAXWELL, G. M., AND YOUNG, W. P. Isolated mitral stenosis in an infant of three months: report of a case treated surgically, 787
MITCHELL, AVARD M., SACKETT, CHARLES H., HUNZICKER, WARREN J., AND LEVINE, SAMUEL A. The clinical features of aortic stenosis, 684
MITCHELL, JERE H., AND SHAPIRO, ALVIN P. The relationship of Adrenalin and T-wave changes in the anxiety state, 323
MOSER, MARVIN. (*See* Sayer, Moser, and Mattingly), 42
MOSES, CAMPBELL. The effect of phosphorylated hesperidin on experimental atherosclerosis, 264
MOYER, JOHN H., AND HANDLEY, CARROLL A. Blood pressure and renal hemodynamic responses to Aramine and the alterations of these responses by adrenergic blockade with Dibenzyline, 173
——, LIVESAY, W. R., AND SEIBERT, RICHARD A. The effect of blood pressure reduction with Arfonad on renal hemodynamics and excretion of water and electrolytes, 817
——. (*See* Ford, Livesay, Spurr, and Moyer), 123

N

NADAS, ALEXANDER S. (*See* Rudolph, Nadas, and Goodale), 808
NEUBUERGER, KARL T. (*See* Denst, Edwards, Neubuerger, and Blount), 506
NYE, ROBERT E., JR. (*See* Yu, Lovejoy, Joos, Nye, and Beatty), 544

O

O'HARE, JAMES P. (*See* Friend, O'Hare, and Levine), 775
OSTRICH, RALPH. (*See* Smith, Rosenbaum, and Ostrich), 847

P

PASCALE, LUKE R., BERNSTEIN, LIONEL M., SCHOOLMAN, HAROLD M., AND FOLEY, EDMUND F. Intravenous procaine amide in the treatment of cardiac arrhythmias, 110
——. (*See* Bernstein, Pascale, Schoolman, and Foley), 82
PERÄSALO, O., AND KYLLÖNEN, K. E. J. A congenital subclavian arteriovenous fistula and a truncus brachiocephalicus totalis in the same patient, 465
PERRY, W. F. (*See* Beamish, Perry, and Storrie), 433
PLATTS, MARGARET M., AND WHITAKER, WILLIAM. The diagnostic importance of the blood carbon dioxide content of patients with central cyanosis, 77
PRINZMETAL, MYRON. (*See* Rakita, Borduas, Rothman, and Prinzmetal), 351

R

RAKITA, LOUIS, BORDUAS, JEAN LOUIS, ROTHMAN, SOL, AND PRINZMETAL, MYRON. Studies on the mechanism of ventricular activity. XII. Early changes in the RS-T segment and QRS complex following acute coronary artery occlusion: experimental study and clinical applications, 351
RAY, C. T. (*See* Burch and Ray), 373
RICHMOND, GLENN H. (*See* Walker and Richmond), 275
RIESZ, R. R. (*See* Geckeler, Likoff, Mason, Riesz, and Wirth), 189
RIZZO, NICHOLAS D. (*See* Fox, Rizzo, and Gifford), 645
RODBARD, S., AND WILLIAMS, F. The dynamics of mitral insufficiency, 521
ROMANS, WILLIAM E. (*See* Brody, McKay, and Romans), 589
ROSENBAUM, ROBERT. (*See* Smith, Rosenbaum, and Ostrich), 847
ROTH, FRITZ. (*See* Scherf, Blumenfeld, Golbey, Ladopoulos, and Roth), 573
ROTHE, CARL F., AND SAPIRSTEIN, LEO A. A rapid blood sample collector for use in the determination of cardiac output, 141
ROTHMAN, SOL. (*See* Rakita, Borduas, Rothman, and Prinzmetal), 351
RUDOLPH, ABRAHAM M., NADAS, ALEXANDER S., AND GOODALE, WALTER T. Intracardiac left-to-right shunt with pulmonic stenosis, 808
RUSHMER, ROBERT F., TIDWELL, ROBERT A., AND ELLIS, RICHARD M. Sonvelographic recording of murmurs during acute myocarditis, 835

S

SACKETT, CHARLES H. (*See* Mitchell, Sackett, Hunzicker, and Levine), 684
SADOFF, CHARLES. (*See* Wilson, Hoseth, Sadoff, and Dempsey), 671
SAPIN, SAMUEL O. (*See* Kuhn, Donoso, and Sapin), 280
SAPIRSTEIN, LEO A. (*See* Rothe and Sapirstein), 141
SARNOFF, STANLEY J. (*See* Isaacs, Berglund, and Sarnoff), 66
SAYER, WILLIAM J., MOSER, MARVIN, AND MATTINGLY, THOMAS W. Pheochromocytoma and the abnormal electrocardiogram, 42
SCHACK, JEROME A. (*See* Tannenbaum, Vesell, and Schack), 562
SCHERF, DAVID, BLUMENFELD, SERGE, GOLBEY, MAURICE, LADOPOULOS, CONSTANTINE, AND ROTH, FRITZ. Experimental ectopic cardiac rhythms, 573
SCHMOCK, C. L. (*See* Schumacher and Schmock), 933
SCHOOLMAN, HAROLD M. (*See* Bernstein, Pascale, Schoolman, and Foley), 82
——. (*See* Pascale, Bernstein, Schoolman, and Foley), 110

SCHUMACHER, E. E., Jr., AND SCHMOCK, C. L. The control of certain cardiac arrhythmias with isopropylnorepinephrine, 933
SCHWARTZ, SIDNEY P., AND HALLINGER, LEONARD N. Transient ventricular fibrillation, 390
SCHWARZSCHILD, MYRON M., HOFFMAN, IRWIN, AND KISSIN, MILTON. Errors in unipolar limb leads caused by unbalanced skin resistances, and a device for their elimination, 235
SCOTT, RALPH C. (*See* Simon, Iglauer, and Scott), 624
SEIBERT, RICHARD A. (*See* Moyer, Livesay, and Seibert), 817
SEKELJ, PAUL. Further studies on oximetry, 746
SHACKMAN, N. H. (*See* Kroop, Heffer, and Shackman), 612
SHACKMAN, NATHAN H., HEFFER, ERNEST T., AND KROOP, IRVING G. The C-reactive protein determination as a measure of rheumatic activity, 599
SHAPIRO, ALVIN P. (*See* Mitchell and Shapiro), 323
SHAW, J. M. (*See* Colbeck and Shaw), 270
SILVERMAN, JACOB J. (*See* Talbot and Silverman), 146
SIMON, DAVID L., IGLAUER, ARNOLD, AND BRAUNSTEIN, JOHN. The immediate effect of cigarettes on the circulation of healthy and habitual male smokers, 185
——, ——, AND SCOTT, RALPH C. Studies on the use of ethaverine in the treatment of angina pectoris, 624
SIMON, M. A., AND LIU, S. F. Calcification of the mitral valve annulus and its relation to functional valvular disturbance, 497
SLETTEN, IVAN W. (*See* Tuchman, Sletten, and Crumpton), 449
SMITH, J. E., ROSENBAUM, ROBERT, AND OSTRICH, RALPH. Studies with the displacement, velocity, and acceleration ballistocardiograph in aortic insufficiency, 847
SOBIN, SIDNEY S., CARSON, MERL J., JOHNSON, JOHN L., AND BAKER, CHARLES R. Pulmonary valvular stenosis with intact ventricular septum: isolated valvular stenosis and valvular stenosis associated with interatrial shunt, 416
SPRENGEL, REUBEN A., AND BROWN, ALBERT F. Aortic septum defect, 796
SPURR, CHARLES. (*See* Ford, Livesay, Spurr, and Moyer), 123
STEMBRIDGE, VERNIE A., HEJTMANCIK, MILTON R., AND HERRMANN, GEORGE R. Unusual musical murmurs of anterior cusp aortic regurgitation, 163
STEWART, HAROLD J., AND CARR, HENRY A. The anoxemia test, 293
STORRIE, V. MARIE. (*See* Beamish, Perry, and Storrie), 433
SWAN, HENRY. (*See* McCord, Swan, and Blount), 405

T

TACKET, HALL S. (*See* Little, Brody, and Tacket), 721
TALBOT, THEODORE J., AND SILVERMAN, JACOB J. Pulmonary artery enlargement simulating a neoplasm of the lung, 146
TANNENBAUM, OSCAR, VESELL, HARRY, AND SCHACK, JEROME A. The spatial vectorballistocardiogram, 562
TAYLOR, HENRY LONGSTREET, MALONEY, WILLIAM F., AND KEYS, ANCEL. Factors affecting the low-frequency, critically-damped ballistocardiogram, with special reference to age, body size, and body composition, 864
TIDWELL, ROBERT A. (*See* Rushmer, Tidwell, and Ellis), 835
TOBIN, MICHAEL. (*See* Edson, Flamm, Dickes, Tobin, and Loeb), 897
TOLHOEK, H. A. (*See* Burger, Tolhoek, and Backbier), 249
TUCHMAN, HERMAN, SLETTEN, IVAN W., AND CRUMPTON, CHARLES W. A clinical study of the effects of intravenous reserpine (Serpasil) in hypertensive patients, 449

U

UGGLA, LARS-GUSTAF. (*See* Björk, Malmström, and Uggla), 8

V

VAKIL, RUSTOM JAL. Accelerated auriculoventricular nodal conduction as a transitory phenomenon in a nervous patient, 157
——. Heart disease in India, 439
VAN DER TWEEL, L. H. (*See* Durrer, van der Tweel, and Blickman), 13
VANDERKOLK, KENNETH, DONTAS, A. S., AND HOOBLER, S. W. Renal and hypotensive effects of acute and chronic oral treatment with 1-Hydrazinophthalazine (Apresoline) in hypertension, 95
VESELL, HARRY. (*See* Tannenbaum, Vesell, and Schack), 562

W

WALKER, WELDON J., AND RICHMOND, GLENN H. Posterior ventricular aneurysm in patients with dextrocardia and situs inversus, 275
WASSERBURGER, RICHARD H. (*See* Korst and Wasserburger), 383
WELLS, P. V. Flarimeter tests on athletes, 914
WERKÖ, LARS. (*See* Ek, Bucht, and Werkö), 102
WHITAKER, WILLIAM. (*See* Chesterman and Whitaker), 631
——. (*See* Platts and Whitaker), 77
WILLIAMS, F. (*See* Rodbard and Williams), 521

WILSON, RUSSELL H., HOSETH, WAYNE, SADOFF, CHARLES, AND DEMPSEY, MARY E. Pathologic physiology and diagnostic significance of the pressure pulse tracings in the heart in patients with constrictive pericarditis and pericardial effusion, 671

WIRTH, CHARLES H. (*See* Geckeler, Likoff, Mason, Riesz, and Wirth), 189

WREN, ESME M. The portal venous pressure in organic heart disease, 929.

Y

YOUNG, W. P. (*See* Maxwell and Young), 787

YU, PAUL N., LOVEJOY, F. W., JR., JOOS, HOWARD A., NYE, ROBERT E., JR., and BEATTY, DAVID C. Studies of pulmonary hypertension. V, 544

Z

ZUIDEMA, P. J. Dissociation with double interference, 475

SUBJECT INDEX

A

Abdomen, effect of pressure over hepatic region of, upon venous pressure (Burch and Ray), 376

Acceleration, displacement, velocity, and, ballistocardiograph, studies with, in aortic insufficiency (Smith et al.), 847

Activation, spread of in left ventricular wall of dog. III (Durrer et al.), 13

Adrenalin and T-wave changes, relationship of, in anxiety state (Mitchell and Shapiro), 323

Adrenergic blockade with Dibenzyline, blood pressure and renal hemodynamic responses to Aramine and alterations of these responses by (Moyer and Handley), 173

Age, body size, and body composition, factors affecting low-frequency, critically-damped ballistocardiogram, with special reference to (Taylor et al.), 864

Algebraic, vector and relationship of CF and V chest leads (Douglas and Cohen), 340

Ammonium chloride, comparative diuretic effectiveness of mercumatilin and meralluride with and without concomitant administration of (Batterman), 780

Aneurysm, coronary, with arteriovenous fistula (Colbeck and Shaw), 270

ventricular, posterior, in patient with dextrocardia and situs inversus (Walker and Richmond), 275

Angina pectoris, action of triethanolamine trinitrate in (Friend et al.), 775

provocative aspects of lipotrophic therapy in (Goulder et al.), 906

studies on use of ethaverine in treatment of (Simon et al.), 624

Anginal pain, relation between electrocardiographic changes during anoxemia test and (Stewart and Carr), 306

Announcements, 322, 484, 644, 800

Annulus, mitral valve, calcification of, and its relation to functional valvular disturbance (Simon and Liu), 497

Anoxemia test (Stewart and Carr), 293

and anginal pain, relation between electrocardiographic changes during (Stewart and Carr), 306

autopsy reports in patients who have had (Stewart and Carr), 313

changes in Q-T interval during (Stewart and Carr), 301

electrocardiographic changes occurring during, in patients with heart disease and in patients with diseases other than coronary artery disease (Stewart and Carr), 304

physiologic observations during, and recent observations (Stewart and Carr), 303

Anoxemia test (Stewart and Carr)—Cont'd

precautions to be followed in carrying out (Stewart and Carr), 299

techniques other than Levy's for (Stewart and Carr), 300

use of, in evaluation of effects of drugs (Stewart and Carr), 315

value of, as guide to prognosis in coronary artery disease (Stewart and Carr), 312

for diagnosis of coronary artery disease (Stewart and Carr), 307

tests, arterial oxygen saturation prevailing during (Stewart and Carr), 302

untoward reactions, accidents, and deaths during (Stewart and Carr), 299

Anoxia, normal and abnormal changes in electrocardiogram with (Stewart and Carr), 296

Anterior cusp aortic regurgitation, unusual musical murmurs of (Stembridge et al.), 163

Anxiety state, relationship of Adrenalin and T-wave changes in (Mitchell and Shapiro), 323

Aorta, study of correlation between roentgenographic and post-mortem calcification of (Hyman and Epstein), 540

Aortic electrokymogram in normal subjects and patients with syphilitic aortic insufficiency (Brandfonbrener and Eisenberg), 54

insufficiency, analysis of ten cases of (Smith et al.), 854

studies with displacement, velocity, and acceleration ballistocardiograph in (Smith et al.), 847

regurgitation, anterior cusp, unusual musical murmurs of (Stembridge et al.), 163

septum defect (Sprengel and Brown), 796

stenosis, calcific: study of serum cholesterol (Boas et al.), 485

classification of lesions (Mitchell et al.), 686

clinical features of (Mitchell et al.), 684

complications and sequelae of (Mitchell et al.), 692

criteria for diagnosis of (Boas et al.), 486

electrocardiographic findings (Mitchell et al.), 699

etiology (Mitchell et al.), 687

life expectancy (Mitchell et al.), 689

past history of rheumatic fever (Mitchell et al.), 688

physical findings (Mitchell et al.), 702

sex distribution (Mitchell et al.), 689

Aramine, blood pressure and renal hemodynamic responses to, and alterations of responses by adrenergic blockade with Dibenzyline (Moyer and Handley), 173

Arfonad, effect of blood pressure reduction with, on renal hemodynamics and excretion of water and electrolytes (Moyer et al.), 817
on water and electrolyte excretion (Table II) (Moyer et al.), 821
of norepinephrine on water and electrolyte excretion in patients previously made hypotensive with (Table IV) (Moyer et al.), 823
renal hemodynamic response to norepinephrine when blood pressure was previously reduced with (Table III) (Moyer et al.), 822
Arrhythmias, cardiac, certain, control of, with isopropylnorepinephrine (Schumacher and Schmock), 933
intravenous procaine amide in treatment of (Pascale et al.), 110
Arterial embolism, late mitral commissurotomy followed by (Grossman et al.), 471
hypertension, influence of rapid infusion of glucose on renal dynamics and sodium excretion in patients with (Ek et al.), 102
Arteriovenous fistula, coronary aneurysm with (Colbeck and Shaw), 270
subclavian, congenital, and truncus brachiocephalicus totalis in same patient (Perasälo and Kyllönen), 465
Artery, cardiac and pulmonary, pressure pulses in experimental mitral stenosis (Lasser and Loewe), 801
coronary, left, in dog, patterns of anterior descending branch of (Craig and Learned), 455
pulmonary, enlargement simulating neoplasm of lung (Talbot and Silverman), 146
right main, superior vena cava obstruction with complete obstruction of (Briggs et al.), 288
systemic, comparison of oxygen tension in blood from left atrium and (Björk et al.), 8
Atherosclerosis, experimental, effect of phosphorylated hesperidin on (Moses), 264
Athletes, flarimeter tests on (Wells), 914
Atrial appendages, biopsies of lung and, in mitral stenosis: correlation of data from cardiac catheterization with pulmonary vascular lesions (Denst et al.), 506
flutter: 1 to 1 conduction during treatment with quinidine and digitalis (London and Howell), 152
thrombosis, left, massive, and recurring pleural effusion (Dorney and Cabaud), 459
Atrioventricular conduction, prolonged depression of, caused by large dosages of protoveratrine (Black and Lyons), 266
Atrium, left, and systemic artery, comparison of oxygen tension in blood from (Björk et al.), 8
Auricular flutter associated with complete heart block (Korst and Wasserburger), 383
association of Wenckebach phenomenon with (Brotmacher), 629
effect of intravenously administered procaine amide on (Table II) (Pascale et al.), 114
with bundle branch block, intravenous procaine amide as aid to differentiate, from paroxysmal ventricular tachycardia (Bernstein et al.), 82
tachycardia with Wenckebach phenomenon occurring during course of cardiac catheterization (Kuhn et al.), 280
Auriculoventricular dissociation, established, observations on peripheral arterial pulse pressures in course of transient ventricular fibrillation during (VI); transient ventricular fibrillation (Schwartz and Hallinger), 390
nodal conduction, accelerated, as transitory phenomenon in nervous patient (Vakil), 157
Axis, electrical, mathematical method to determine magnitude of (Ayala y de Landero), 894
Axostat I (Brody et al.), 589
Axostat II (Little et al.), 721

B

Ballistocardiogram, critically-damped, low-frequency, factors affecting, with special reference to age, body size, and body composition (Taylor et al.), 864
Ballistocardiograph, displacement, velocity, and acceleration, studies with, in aortic insufficiency (Smith et al.), 847
standards, normal, for 50 normal adults between 20 and 40 years of age (Smith et al.), 849
Ballistocardiographic measurements, effects of age on (Table IV) (Taylor et al.), 870
Ballistocardiography, thoracic (Edson et al.), 897
Biopsies of lung and atrial appendages in mitral stenosis: correlation of data from cardiac catheterization with pulmonary vascular lesions (Denst et al.), 506
Blood carbon dioxide content of patients with central cyanosis, diagnostic importance of (Platts and Whitaker), 77
from left atrium and systemic artery, comparison of oxygen tension in (Björk et al.), 8
pressure and clinical response to intramuscular Veriloid-in-Oil (Table I) (Ford et al.), 124
and renal hemodynamic responses to Aramine and alterations of responses by adrenergic blockade with Dibenzyline (Moyer and Handley), 173

Blood, pressure—Cont'd
reduction (with Arfonad), effect of, on glomerular filtration rate and renal plasma flow (Table IB) (Moyer et al.), 820
on renal hemodynamics and excretion of water and electrolytes (Moyer et al.), 817
on water and electrolyte excretion (Table II) (Moyer et al.), 821
response of patients receiving reserpine (Serpasil) and sodium amytal test (Tuchman et al.), 450
pulmonary, distribution and oxygen diffusion in mitral stenosis (Fowler et al.), 1
sample collector, rapid, for use in determination of cardiac output (Rothe and Sapirstein), 141
Body composition, factors affecting low-frequency, critically-damped ballistocardiogram, with special reference to age, body size and (Taylor et al.), 864
Book reviews, 162, 482, 641, 799
Bundle branch block, intravenous procaine amide as aid to differentiate auricular flutter with, from paroxysmal ventricular tachycardia (Bernstein et al.), 82
Burger triangle, meaning of lead vectors and (Brody), 730

C

Calcification of mitral valve annulus and its relation to functional valvular disturbance (Simon and Liu), 497
roentgenographic and post-mortem, of aorta, study of correlation between (Hyman and Epstein), 540
Carbon dioxide, blood, content of patients with central cyanosis, diagnostic importance of (Platts and Whitaker), 77
Cardiac and pulmonary artery pressure pulses in experimental mitral stenosis (Lasser and Loewe), 801
arrhythmias, certain, control of, with isopropylnorepinephrine (Schumacher and Schmock), 933
intravenous procaine amide in treatment of (Pascale et al.), 110
catheterization, auricular tachycardia with Wenckebach phenomenon occurring during course of (Kuhn et al.), 280
correlation of data from, with pulmonary vascular lesions; biopsies of lung and atrial appendages in mitral stenosis (Denst et al.), 506
output, rapid blood sample collector for use in determination of (Rothe and Sapirstein), 141
resuscitation, manual on, 162 (B. Rev.)
rhythms, ectopic, experimental (Scherf et al.), 573
tamponade, acute, pathologic physiology of, studied by means of ventricular function curves (III); ventricular function curves (Isaacs et al.), 66
Cardiospectrograms (Geckeler et al.), 189
Catheterization, cardiac, auricular tachycardia with Wenckebach phenomenon occurring during course of (Kuhn et al.), 280
correlation of data from, with pulmonary vascular lesions; biopsies of lung and atrial appendages in mitral stenosis (Denst et al.), 506
results of (Table I) (Chesterman and and Whitaker), 632
right heart, data from 10 patients with constrictive pericarditis and 3 patients with pericardial effusion (Table I) (Wilson et al.), 672
Chest leads, CF and V, vector and algebraic relationship of (Douglas and Cohen), 340
Cholesterol, serum, study of; calcific aortic stenosis (Boas et al.), 485
CF and V chest leads, vector and algebraic relationship of (Douglas and Cohen), 340
Cigarettes, immediate effect of, on circulation of healthy and habitual male smokers (Simon et al.), 185
low nicotine (filtered) and regular, statistical comparison of changes in skin temperature produced by smoking (Table I) (Simon et al.), 187
Circuit, equivalent, for human heart-body electrical system (Frank), 738
Circulation of healthy and habitual male smokers, immediate effect of cigarettes on (Simon et al.), 185
Collector, blood sample, rapid, for use in determination of cardiac output (Rothe and Sapirstein), 141
Commissurotomy, mitral, followed by late arterial embolism (Grossman et al.), 471
Conduction, atrioventricular, prolonged depression of, caused by large dosages of protoveratrine (Black and Lyons), 266
1 to 1, during treatment with quinidine and digitalis: atrial flutter (London and Howell), 152
nodal, auriculoventricular, accelerated, as transitory phenomenon in nervous patient (Vakil), 157
Congestive heart failure, mechanism of hepatojugular reflux test in (Burch and Ray), 373
Coronary aneurysm with arteriovenous fistula (Colbeck and Shaw), 270
artery disease, value of anoxemia test for diagnosis of (Stewart and Carr), 307
left, in dog, patterns of anterior descending branch of (Craig and Learned), 455
ligation, epicardial leads after (Rakita et al.), 359
intramural and cavity leads after (Rakita et al.), 360
occlusion, acute, early changes in RS-T segment and QRS complex following: experimental study and clinical applications (XII); studies on mechanism of ventricular activity (Rakita et al.), 351

Coronary—Cont'd
insufficiency, methods, other than anoxemia test, for detection of (Stewart and Carr), 314
C-reactive protein determination as measure of rheumatic activity (Shackman et al.), 599
Cusp, anterior, aortic regurgitation, unusual musical murmurs of (Stembridge et al.), 163
Cyanosis, central, diagnostic importance of blood carbon dioxide content of patients with (Platts and Whitaker), 77

D

Dextrocardia and situs inversus, posterior ventricular aneurysm in patient with (Walker and Richmond), 275
Dibenzyline, blood pressure and renal hemodynamic responses to Aramine and alterations of responses by adrenergic blockade with (Moyer and Handley), 173
Digitalis, 1 to 1 conduction during treatment with quinidine and: atrial flutter (London and Howell), 152
Displacement, velocity, and acceleration ballistocardiograph, studies with, in aortic insufficiency (Smith et al.), 847
Dissociation with double interference (Zuidema), 475
Diuretic effectiveness, comparative, of mercumatilin and meralluride with and without concomitant administration of ammonium chloride (Batterman), 780
Dog, patterns of anterior descending branch of left coronary artery in (Craig and Learned), 455
spread of activation in left ventricular wall of (Durrer et al.), 13
Drugs, use of anoxemia test in evaluation of effects of (Stewart and Carr), 315

E

Ectopic cardiac rhythms, experimental (Scherf et al.), 573
Effusion, pericardial, pathologic physiology and diagnostic significance of pressure pulse tracings in heart in patients with constrictive pericarditis and (Wilson et al.), 671
pleural, recurring, massive left atrial thrombosis and (Dorney and Cabaud), 459
Einführung in die Vektorielle Deutung des EKG, 642 (B. Rev.)
EKG, Einführung in Vektorielle Deutung des, 642 (B. Rev.)
Electrical axis, mathematical method to determine magnitude of (Ayala y de Landero), 894
system, human heart-body, equivalent circuit for (Frank), 738
Electrocardiogram, abnormal, pheochromocytoma and (Sayer et al.), 42
normal and abnormal changes in, with anoxia (Stewart and Carr), 296
Electrocardiograms, extremity, new instrument for multiaxial registration of (I); axostat (Brody et al.), 589
Electrocardiographic changes during anoxemia test and anginal pain, relation between (Stewart and Carr), 306
occurring during anoxemia test in patients with heart disease and in patients with diseases other than coronary artery disease (Stewart and Carr), 304
findings: aortic stenosis (Mitchell et al.), 699
Electrocardiography, practical, 162 (B. Rev.)
Electrodes, needle, experiments with; activation in ventricular wall of dog (Durrer et al.), 22
Electrokymogram, aortic, in normal subjects and patients with syphilitic aortic insufficiency (Brandfonbrener and Eisenberg), 54
Electrolytes, excretion of water and, effect of blood pressure reduction with Arfonad on renal hemodynamics and (Moyer et al.), 817
Electrophoresis in rheumatic fever, evaluation of (Kroop et al.), 612
Elektrische Herzbild, 641 (B. Rev.)
Embolism, arterial, late, mitral commissurotomy followed by (Grossman et al.), 471
Endocarditis, enterococcal, of prolonged duration, cure of (Krapin), 792
Enterococcal endocarditis of prolonged duration, cure of (Krapin), 792
Equivalent circuit for human heart-body electrical system (Frank), 738
Ethaverine, studies on use of, in treatment of angina pectoris (Simon et al.), 624
Extremity electrocardiograms, new instrument for multiaxial registration of (I); axostat (Brody et al.), 589

F

Familial xanthomatosis and hypercholesteremia, observations on calcific aortic stenosis in; calcific aortic stenosis: study of serum cholesterol (Boas et al.), 485
Fibrillary process in man, transient ventricular fibrillation (Schwartz and Hallinger), 397
Fibrillation, ventricular, transient (Schwartz and Hallinger), 390
Fistula, arteriovenous, coronary aneurysm with (Colbeck and Shaw), 270
subclavian, congenital, and truncus brachiocephalicus totalis in same patient (Peräsalo and Kyllönen), 465
Flarimeter tests on athletes (Wells), 914
abdominal contraction (Wells), 917
correlation with physical condition (Wells), 925
flow index (Wells), 919
responses to standard stimulus (Wells), 917
standard technique for (Wells), 915

Flutter, atrial: 1 to 1 conduction during treatment with quinidine and digitalis (London and Howell), 152
auricular, associated with complete heart block (Korst and Wasserburger), 383
association of Wenckebach phenomenon with (Brotmacher), 629
with bundle branch block, intravenous procaine amide as aid to differentiate, from paroxysmal ventricular tachycardia (Bernstein et al.), 82

G

Gehirn, Kreislauf and: Tagung. Hauptthema; Verhandlungen der Deutschen Gesellschaft für Kreislaufforschung, 482 (B. Rev.)
Glucose, influence of rapid infusion of, on renal dynamics and sodium excretion in patients with arterial hypertension (Ek et al.), 102

H

H wave, relationship of, in headward-footward axis to motion of body in lateral and anteroposterior axes (Table I) (Tannenbaum et al.), 568
Heart block, complete, auricular flutter associated with (Korst and Wasserburger), 383
disease, electrocardiographic changes occurring during anoxemia test in patients with; and in patients with diseases other than coronary artery disease (Stewart and Carr), 304
in India (Vakil), 439
chronic cor pulmonale (Vakil), 447
coronary heart disease (Vakil), 446
hypertensive heart disease (Vakil), 445
rheumatic group (Vakil), 442
syphilitic heart disease (Vakil), 444
organic, portal venous pressure in (Wren), 929
rheumatic, idiopathic myocardial hypertrophy simulating (Levin and Cohen), 637
diseases, uncommon, 800 (B. Rev.)
failure, congestive, chronic; hepatojugular reflex test (Burch and Ray), 377
mechanism of hepatojugular reflux test in (Burch and Ray), 373
pathologic physiology and diagnostic significance of pressure pulse tracings in, in patients with constrictive pericarditis and pericardial effusion (Wilson et al.), 671
vector, potential distribution on body surface caused by (Burger et al.), 249
Heart-body human electrical system, equivalent circuit for (Frank), 738
Hemodynamic responses, renal, to Aramine, blood pressure and, and alterations of responses by adrenergic blockade with Dibenzyline (Moyer and Handley), 173
Hemodynamics, renal, and excretion of water and electrolytes, effect of blood pressure reduction with Arfonad on (Moyer et al.), 817
Hepatic region of abdomen, effect of pressure over, upon venous pressure (Burch and Ray), 376
Hepatojuglar reflux test, mechanism of, in congestive heart failure (Burch and Ray), 373
Herzbild, Elektrische, 641 (B. Rev.)
Hesperidin, phosphorylated, effect of, on experimental atherosclerosis (Moses), 264
1-Hydrazinophthalazine (Apresoline), renal and hypotensive effects of acute and chronic oral treatment with, in hypertension (VanderKolk et al.), 95
Hypercholesteremia, observations on calcific aortic stenosis in familial xanthomatosis and; calcific aortic stenosis: study of serum cholesterol (Boas et al.), 485
Hypertension, arterial, influence of rapid infusion of glucose on renal dynamics and sodium excretion in patients with (Ek et al.), 102
pulmonary, studies of, V (Yu et al.), 544
renal and hypotensive effects of acute and chronic oral treatment with 1-Hydrazinophthalazine (Apresoline) in (VanderKolk et al.), 95
Hypertensive emergencies, treatment of: use of Veriloid-in-Oil intramuscularly (Ford et al.), 123
patients, clinical study of effects of intravenous reserpine (Serpasil) in (Tuchman et al.), 449
treated with potassium thiocyanate, observations on thyroid function in (Beamish et al.), 433
Hypertrophy, myocardial, idiopathic, simulating rheumatic heart disease (Levin and Cohen), 637
Hypotensive, renal and, effects of acute and chronic oral treatment with 1-Hydrazinophthalazine (Apresoline) in hypertension (VanderKolk et al.), 95

I

I wave, relationship of, in headward-footward axis to motion of body in lateral and anteroposterior axes (Table II) (Tannenbaum et al.), 569
Image surface, examples of use of (Burger et al.), 256
geometrical representation by means of (Burger et al.), 250
India, heart disease in (Vakil), 439
Infant of three months, isolated mitral stenosis in: report of case treated surgically (Maxwell and Young), 787
Insufficiency, aortic, studies with displacement, velocity, and acceleration ballistocardiograph in (Smith et al.), 847
syphilitic, aortic electrokymogram in normal subjects and patients with (Brandfonbrener and Eisenberg), 54

Insufficiency—Cont'd
mitral, dynamics of (Rodbard and Williams), 521
Interatrial shunt, isolated valvular stenosis and valvular stenosis associated with; pulmonary valvular stenosis with intact ventricular septum (Sobin et al.), 416
Interventricular septum, perforation of (Goetz and Gropper), 130
Intracardiac left-to-right shunt with pulmonic stenosis (Rudolph et al.), 808
Isopropylnorepinephrine, control of certain cardiac arrhythmias with (Schumacher and Schmock), 933

J

J wave, relationship of, in headward-footward axis to motion of body in lateral and anteroposterior axes (Table III) (Tannenbaum et al.), 570

K

K wave, relationship of, in headward-footward axis to motion of body in lateral and anteroposterior axes (Table IV) (Tannenbaum et al.), 570
Kreislauf and Gehirn; Tagung Hauptthema. Verhandlungen der Deutschen Gesellschaft für Kreislaufforschung, 482 (B. Rev.)
Kreislaufs, Regulationsprufüng des, 799 (B. Rev.)

L

L wave, relationship of, in headward-footward axis to motion of body in lateral and anteroposterior axes (Table V) (Tannenbaum et al.), 571
Lead vectors and Burger triangle, meaning of (Brody), 730
−VR and rational arrangement of limb leads; unipolar value of standard limb leads (Fumagalli), 204
Leads, chest, CF and V, vector and algebraic relationship of (Douglas and Cohen), 340
epicardial, after coronary artery ligation (Rakita et al.), 359
intramural and cavity, after coronary artery ligation (Rakita et al.), 360
limb, quantitative estimation of ventricular strain in (Gross), 881
standard, unipolar value of: Lead −VR and rational arrangement of limb leads (Fumagalli), 204
unipolar, errors in, caused by unbalanced skin resistances, and device for elimination (Schwarzschild et al.), 235
precordial, right, elevation of RS-T segment, apparent or real, in, as probable normal variant (Edeiken), 331
transmural; activation in ventricular wall of dog (Durrer et al.), 15
Limb leads, quantitative estimation of ventricular strain in (Gross), 881
standard, unipolar value of: Lead −VR and rational arrangement of limb leads (Fumagalli), 204
unipolar, errors in, caused by unbalanced skin resistances, and device for elimination (Schwarzschild et al.), 235
Lipotropic therapy, changes in serum cholesterol concentrations (mg. per cent) during, in subjects showing clinical improvement (Table I) (Goulder et al.), 908
lipid phosphorus concentrations (mg. per cent) during, in subjects showing clinical improvement (Table II) (Goulder et al), 909
serum phospholipid ratio (per cent) during, in subjects showing clinical improvement (Table III) (Goulder et al.), 909
provocative aspects of, in angina pectoris (Goulder et al.), 906
Lung and atrial appendages, biopsies of, in mitral stenosis: correlation of data from cardiac catheterization with pulmonary vascular lesions (Denst et al.), 506
pulmonary artery enlargement simulating neoplasm of (Talbot and Silverman), 146

M

Meralluride, comparative diuretic effectiveness of mercumatilin and, with and without concomitant administration of ammonium chloride (Batterman), 780
Mercumatilin and meralluride, comparative diuretic effectiveness of, with and without concomitant administration of ammonium chloride (Batterman), 780
Mitral and tricuspid valvotomy for mitral and tricuspid stenosis (Chesterman and Whitaker), 631
commissurotomy followed by late arterial embolism (Grossman et al.), 471
insufficiency, dynamics of (Rodbard and Williams), 521
stenosis, biopsies of lung and atrial appendages in: correlation of data from cardiac catheterization with pulmonary vascular lesions (Denst et al.), 506
experimental, cardiac and pulmonary artery pressure pulses in (Lasser and Loewe), 801
isolated, in infant of three months: report of case treated surgically (Maxwell and Young), 787
pulmonary blood distribution and oxygen diffusion in (Fowler et al.), 1
simultaneous pressure measurements in left ventricle and brachial artery in; simultaneous catheterization of left and right side of heart (Table I) (Björk et al.), 199

Mitral and tricuspid—Cont'd
surgery, psychological observations of patients undergoing (Fox et al.), 645
valve annulus, calcification of, and its relation to functional valvular disturbance (Simon and Liu), 497
Murmurs, musical, unusual, of anterior cusp aortic regurgitation (Stembridge et al.), 163
Myocardial hypertrophy, idiopathic, simulating rheumatic heart disease (Levin and Cohen), 637
Myocarditis, acute, sonvelographic recording of murmurs during (Rushmer et al.), 835

N

Needle electrodes, experiments with; activation in ventricular wall of dog (Durrer et al.), 22
Neoplasm of lung, pulmonary artery enlargement simulating (Talbot and Silverman), 146
Nervous patient, accelerated auriculoventricular nodal conduction as transitory phenomenon in (Vakil), 157
Nodal conduction, auriculoventricular, accelerated, as transitory phenomenon in nervous patient (Vakil), 157
Node, sinuatrial, in rat (King), 785
Norepinephrine, effect of, on water and electrolyte excretion in patients previously made hypotensive with Arfonad (Table IV) (Moyer et al.), 823

O

Occlusion, coronary, artery, acute, early changes in RS-T segment and QRS complex following experimental study and clinical applications (XII); studies on mechanism of ventricular activity (Rakita et al.), 351
Output, cardiac, rapid blood sample collector for use in determination of (Rothe and Sapirstein), 141
Oximeter, direct-writing (Sekelj), 757
Oximetry, further studies on (Sekelj), 746
Oxygen diffusion, pulmonary blood distribution and, in mitral stenosis (Fowler et al.), 1
saturation, arterial, prevailing during anoxemia tests (Stewart and Carr), 302
tension, comparison of, in blood from left atrium and systemic artery (Björk et al.), 8

P

P loop of spatial vectorcardiogram, studies of: normal P loop (Fowler and Dorney), 36
Patent ductus arteriosus with marked pulmonary hypertension (V); studies of pulmonary hypertension (Yu et al.), 544
Pericardial effusion, pathologic physiology and diagnostic significance of pressure pulse tracings in heart in patients with constrictive pericarditis and (Wilson et al.), 671
right heart catheterization data from 10 patients with constrictive pericarditis and 3 patients with (Table I) (Wilson et al.), 672
Pericarditis, constrictive, and pericardial effusion, pathologic physiology and diagnostic significance of pressure pulse tracings in patients with (Wilson et al.), 671
right heart catheterization data from 10 patients with, and 3 patients with preicardial effusion (Table I) (Wilson et al.), 672
Pheochromocytoma and abnormal electrocardiogram (Sayer et al.), 42
Phonocardiography, clinical calibration in (Luisada and Gamna), 826
Phosphorylated hesperidin, effect of, on experimental atherosclerosis (Moses), 264
Pleural effusion, recurring, massive left atrial thrombosis and (Dorney and Cabaud), 459
Postfibrillary period, transient ventricular fibrillation (Schwartz and Hallinger), 401
Potassium thiocyanate, observations on thyroid function in hypertensive patients treated with (Beamish et al.), 433
Potential distribution of dipole parallel to axis of infinite cylinder (Burger et al.), 261
perpendicular to axis of infinite cylinder Burger et al.), 262
on body surface caused by heart vector (Burger et al.), 249
on closed (finite) cylinder (Burger et al.), 253
on open (infinite) cylinder (Burger et al.), 250
on two parallel planes (Burger et al.), 256
Potentials of dipoles in finite cylinder: method of electrical images (Burger et al.), 262
Precordial leads, right, elevation of RS-T segment, apparent or real in, as probable normal variant (Edeiken), 331
Prefibrillary period, transient ventricular fibrillation (Schwartz and Hallinger), 392
Pressure, blood, reduction with Arfonad, effect of, on renal hemodynamics and excretion of water and electrolytes (Moyer et al.), 817
pulse tracings, pathologic physiology and diagnostic significance of, in heart in patients with constrictive pericarditis and pericardial effusion (Wilson et al.), 671
pulses, cardiac and pulmonary artery, in experimental mitral stenosis (Lasser and Loewe), 801

Pressure—Cont'd
venous, effect of pressure over hepatic region of abdomen upon (Burch and Ray), 376
portal, in organic heart disease (Wren), 929
ventricular, left, measurement in man (Björk et al.), 197
Pressures, pulse, arterial, peripheral, observations on, in course of transient ventricular fibrillation during established auriculoventricular dissociation (VI); transient ventricular fibrillation (Schwartz and Hallinger), 390
Procaine amide, intravenous, as aid to differentiate auricular flutter with bundle branch block from paroxysmal ventricular tachycardia (Bernstein et al.), 82
in treatment of cardiac arrhythmias (Pascale et al.), 110
Protein, C-reactive, determination as measure of rheumatic activity (Shackman et al.), 599
Protoveratrine, prolonged depression of atrioventricular conduction caused by large dosages of (Black and Lyons), 266
Psychological observations of patients undergoing mitral surgery (Fox et al.), 645
Pulmonary artery enlargement simulating neoplasm of lung (Talbot and Silverman), 146
right main, superior vena cava obstruction with complete obstruction of (Briggs et al.), 288
blood distribution and oxygen diffusion in mitral stenosis (Fowler et al.), 1
cardiac and, artery pressure pulses in experimental mitral stenosis (Lasser and Loewe), 801
hypertension, studies of. V (Yu et al.), 544
valvular stenosis, consideration of specific findings in (Sobin et al.), 428
with intact ventricular septum: isolated valvular stenosis and valvular stenosis associated with interatrial shunt (Sobin et al.), 416
vascular lesions, correlation of data from cardiac catheterization with; biopsies of lung and atrial appendages in mitral stenosis (Denst et al.), 506
Pulmonic stenosis, intracardiac left-to-right shunt with (Rudolph et al.), 808
Pulse, pressure, tracings, pathologic physiology and diagnostic significance of, in heart in patients with constrictive pericarditis and pericardial effusion (Wilson et al.), 671
pressures, arterial, peripheral, observations on, in course of transient ventricular fibrillation during established auriculoventricular dissociation (VI); transient ventricular fibrillation (Schwartz and Hallinger), 390
Pulses, pressure, cardiac and pulmonary artery, in experimental mitral stenosis (Lasser and Loewe), 801

Q

QRS and T vectors, mean, direction of (Helm), 224
complex, early changes in RS-T segment and, following acute coronary artery occlusion: experimental study and clinical applications (XII); studies on mechanism of ventricular activity (Rakita et al.), 351
QRS-wave changes (Rakita et al.), 369
Q-T interval, changes in, during anoxemia test (Stewart and Carr), 301
Quinidine and digitalis, 1 to 1 conduction during treatment with: atrial flutter (London and Howell), 152

R

Rat, sinuatrial node in (King), 785
Regurgitation, aortic, anterior cusp, unusual musical murmurs of (Stembridge et al.), 163
Renal and hypotensive effects of acute and chronic oral treatment with 1-Hydrazinophthalazine (Apresoline) in hypertension (VanderKolk et al.), 95
dynamics and sodium excretion, influence of rapid infusion of glucose on, in patients with arterial hypertension (Ek et al.), 102
hemodynamic response to norepinephrine when blood pressure was previously reduced with Arfonad (Table III) (Moyer et al.), 822
hemodynamics and excretion of water and electrolytes, effect of blood pressure reduction with Arfonad on (Moyer et al.), 817
responses to Aramine, blood pressure and, and alterations of responses by adrenergic blockade with Dibenzyline (Moyer and Handley), 173
Reserpine (Serpasil), intravenous, clinical study of effects of, in hypertensive patients (Tuchman et al.), 449
Resuscitation, cardiac, manual on, 162 (B. Rev.)
Rheumatic activity, C-reactive protein determination as measure of (Shackman et al.), 599
fever, evaluation of electrophoresis in (Kroop et al.), 612
past history of: aortic stenosis (Mitchell et al.), 688
heart disease, idiopathic myocardial hypertrophy simulating (Levin and Cohen), 637
Rhythms, cardiac, ectopic, experimental (Scherf et al.), 573
Roentgenographic and post-mortem calcification of aorta, study of correlation between (Hyman and Epstein), 540

RS-T segment and QRS complex, early changes in, following acute coronary artery occlusion: experimental study and clinical applications (XII); studies on the mechanism of ventricular activity (Rakita et al.), 351
elevation of, apparent or real, in right precordial leads as probable normal variant (Edeiken), 331

S

Septal defect, auricular, pulmonic stenosis, and combined lesions, diagnosis of (Table I) (Rudolph et al.), 811
ventricular, pulmonic stenosis, and combined lesions, diagnosis of (Table II) (Rudolph et al.), 811
Septum, aortic, defect (Sprengel and Brown), 796
interventricular, perforation of (Goetz and Gropper), 130
ventricular, intact, pulmonary valvular stenosis with: isolated valvular stenosis and valvular stenosis associated with interatrial shunt (Sobin et al.), 416
Serum cholesterol, study of; calcific aortic stenosis (Boas et al.), 485
Shunt, interatrial, isolated valvular stenosis and valvular stenosis associated with; pulmonary valvular stenosis with intact ventricular septum (Sobin et al.), 416
left-to-right, intracardiac, with pulmonic stenosis (Rudolph et al.), 808
Sinuatrial node in rat (King), 785
Situs inversus, posterior ventricular aneurysm in patient with dextrocardia and (Walker and Richmond), 275
Size, body, age, and body composition, factors affecting low-frequency, critically-damped ballistocardiogram with special reference to (Taylor et al.), 864
Skin resistances, unbalanced, errors in unipolar limb leads caused by, and device for elimination (Schwarzschild et al.), 235
Smokers, male, healthy and habitual, immediate effect of cigarettes on circulation of (Simon et al.), 185
Sodium excretion, influence of rapid infusion of glucose on renal dynamics and, in patients with arterial hypertension (Ek et al.), 102
Sonvelographic recording of murmurs during acute myocarditis (Rushmer et al.), 835
Spatial vectorballistocardiogram (Tannenbaum et al.), 562
vectorcardiogram, studies of P loop of: normal P loop (Fowler and Dorney), 36
S-T segment displacement (Rakita et al.), 362
Stenosis, aortic, calcific: study of serum cholesterol (Boas et al.), 485
clinical features of (Mitchell et al.), 684
Stenosis—Cont'd
mitral and tricuspid, mitral and tricuspid valvotomy for (Chesterman and Whitaker), 631
biopsies of lung and atrial appendages in: correlation of data from cardiac catheterization with pulmonary vascular lesions (Denst et al.), 506
experimental, cardiac and pulmonary artery pressure pulses in (Lasser and Loewe), 801
isolated, in infant of three months: report of case treated surgically (Maxwell and Young), 787
pulmonary blood distribution and oxygen diffusion in (Fowler et al.), 1
pulmonic, intracardiac left-to-right shunt with (Rudolph et al.), 808
tricuspid: clinical and physiologic evaluation (McCord et al.), 405
valvular, pulmonary, with intact ventricular septum: isolated valvular stenosis and valvular stenosis associated with interatrial shunt (Sobin et al.), 416
Strain, ventricular, in limb leads, quantitative estimation of (Gross), 881
Surgery, mitral, psychological observations of patients undergoing (Fox et al.), 645
Syphilitic aortic insufficiency, aortic electrokymogram in normal subjects and patients with (Brandfonbrener and Eisenberg), 54

T

T, QRS and, vectors, mean, direction of (Helm), 224
Tachycardia, auricular, with Wenckebach phenomenon occurring during course of cardiac catheterization (Kuhn et al.), 280
ventricular, paroxysmal, intravenous procaine amide as aid to differentiate auricular flutter with bundle branch block from (Bernstein et al.), 82
Tachycardias, supraventricular, paroxysmal, effect of intravenously administered procaine amide on (Table I) (Pascale et al.), 112
Tamponade, cardiac, acute, pathologic physiology of, studied by means of ventricular function curves (III); ventricular function (Isaacs et al.), 66
Thoracic ballistocardiography (Edson et al.), 897
Thrombosis, atrial, left, massive, and recurring pleural effusion (Dorney and Cabaud), 459
Thyroid function, observations on, in hypertensive patients treated with potassium thiocyanate (Beamish et al.), 433
Triangle, Burger, meaning of lead vectors and (Brody), 730

Tricuspid, mitral and, valvotomy for mitral and tricuspid stenosis (Chesterman and Whitaker), 631
stenosis: clinical and physiologic evaluation (McCord et al.), 405
Triethanolamine trinitrate, action of, in angina pectoris (Friend et al.), 775
Truncus brachiocephalicus totalis, congenital subclavian arteriovenous fistula and, in same patient (Peräsalo and Kyllönen), 465
T-wave changes, relationship of Adrenalin and, in anxiety state (Mitchell and Shapiro), 323
inversion, massive (Ippolito et al.), 88

U

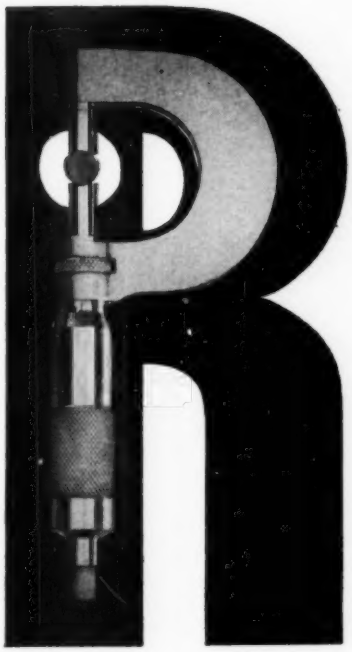
Unipolar limb leads, errors in, caused by unbalanced skin resistances, and device for elimination (Schwarzschild et al.), 235
value of standard limb leads: Lead −VR and rational arrangement of limb leads (Fumagalli), 204

V

V, CF and, chest leads, vector and algebraic relationship of (Douglas and Cohen), 340
Valvotomy, mitral and tricuspid, for mitral and tricuspid stenosis (Chesterman and Whitaker), 631
Valvular disturbance, functional, calcification of mitral valve annulus and its relation to (Simon and Liu), 497
stenosis, pulmonary, consideration of specific findings in (Sobin et al.), 428
with atrial septal defect or patent foramen ovale (Table II) (Sobin et al.), 424
with intact ventricular septum: isolated valvular stenosis and valvular stenosis associated with interatrial shunt (Sobin et al.), 416
Vascular lesions, pulmonary, correlation of data from cardiac catheterization with; biopsies of lung and atrial appendages in mitral stenosis (Denst et al.), 506
Vector and algebraic relationship of CF and V chest leads (Douglas and Cohen), 340
heart, potential distribution on body surface caused by (Burger et al.), 249
Vectorballistocardiogram, spatial (Tannenbaum et al.), 562
Vectorcardiogram, spatial, studies of P loop of: normal P loop (Fowler and Dorney), 36
Vectors, lead, and Burger triangle, meaning of (Brody), 730
Vektorielle Duetung des EKG, Einfuhrung in, 642 (B. Rev.)
Velocity, displacement, and acceleration ballistocardiograph, studies with, in aortic insufficiency (Smith et al.), 847
Vena cava, superior, obstruction with complete obstruction of right main pulmonary artery (Briggs et al.), 288
Venous hypertensive states; hepatojugular reflux test (Burch and Ray), 378
pressure, effect of pressure over hepatic region of abdomen upon (Burch and Ray), 376
portal, in organic heart disease (Wren), 929
Ventricular activity, studies on mechanism of. XII. Early changes in RS-T segment and QRS complex following acute coronary artery occlusion: experimental study and clinical applications (Rakita et al.), 351
aneurysm, posterior, in patient with dextrocardia and situs inversus (Walker and Richmond), 275
fibrillation, transient (Schwartz and Hallinger), 390
postfibrillary period (Schwartz and Hallinger), 401
prefibrillary period (Schwartz and Hallinger), 392
function (Isaacs et al.), 66
pressure measurement, left, in man (Björk et al.), 197
septum, intact, pulmonary valvular stenosis with: isolated valvular stenosis and valvular stenosis associated with interatrial shunt (Sobin et al.), 416
strain in limb leads, quantitative estimation of (Gross), 881
left (Table I) (Gross), 884
right (Table II) (Gross), 886
tachycardia, paroxysmal, effect of intravenously administered procaine amide on (Table III) (Pascale et al.), 116
intravenous procaine amide as aid to differentiate auricular flutter with bundle branch block from (Bernstein et al.), 82
wall, left, of dog, spread of activation in. III (Durrer et al.), 13
Veriloid-in-Oil, use of, intramuscularly; treatment of hypertensive emergencies (Ford et al.), 123

W

Water and electrolytes, excretion of, effect of blood pressure reduction with Arfonad on renal hemodynamics and (Moyer et al.), 817
Wenckebach phenomenon, association of, with auricular flutter (Brotmacher), 629
auricular tachycardia with, occurring during course of cardiac catheterization (Kuhn et al.), 280



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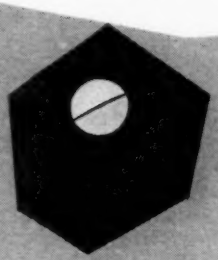

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"Aminophyllin[1] . . . is useful as a peripheral vasodilator and myocardial stimulant for the relief of pulmonary edema or paroxysmal dyspnea of congestive heart failure. Its cardiac effects are more pronounced than those produced by other xanthine derivatives, and in addition to the increase in cardiac output and work of the heart induced by myocardial stimulation, the drug produces a diminution of venous pressure in congestive heart failure."

Symptomatic Relief of Hypertension

Hypertension puts a continuous strain on the myocardium and eventually produces changes in the cardiovascular and renal systems. The actions of Kiophyllin are beneficial in this condition. Moyer and associates[2] found Aminophyllin a most effective agent for relieving headaches resulting from the hypertensive state.

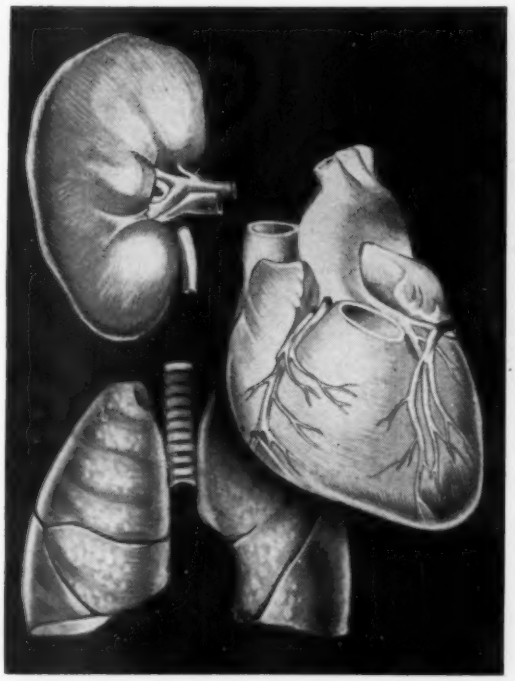
Bronchial and Cardiac Asthma, Emphysema

Among the drugs most effective in relieving swelling of the mucosa and submucosa, increased secretions and spasm of the bronchial muscles, Swineford[3] lists the xanthines, expectorants and sedatives—a combination of drugs as provided in the Kiophyllin formula.

Aminophyllin, the most widely used xanthine, relieves asthma[3] by relaxing constricted bronchi and increasing vital capacity.

Mitchell[4] warns against overmedication with drugs which suppress the cough reflex or have a drying effect on bronchial secretions. Such expectorants as "potassium iodide stimulate[4] the production of thin watery mucus which allows the tenacious plugs to be coughed up more easily."

In the early treatment of emphysema Morledge[5] suggests the use of Aminophyllin and a



"good expectorant cough preparation, especially one containing potassium iodide to keep bronchial secretion loose, ..."

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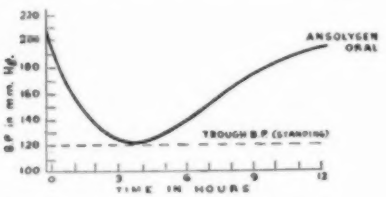
The Drug Used: ANSOLYSEN, a new, orally effective ganglionic blocking agent, which produces certain fall in blood pressure. Drug resistance and by-effects are minimal.

THE TECHNIQUE

The patient's posture influences response. Maximum response is produced when standing, less when sitting, least when recumbent. The physician must determine the dose of ANSOLYSEN required to reduce the patient's standing systolic pressure to normotensive levels for that patient at the point of maximum drug effect.



Dosage: The starting dose is 20 mg., taken orally every 8 hours. The morning dose may be taken before or after breakfast, but the patient should consistently follow the course elected. Each dose is increased by 20 mg. every second day until the patient experiences a little faintness or giddiness in the standing position (postural hypotension) at the time of maximum drug action.[3] The ideal dose is nearly always 20 mg. less than the dose that just succeeds in causing faintness in the standing posture.

Maintenance of Effective Dose: Where several daily recordings of pressure can be made by the patient or a member of his family, the physician can easily adjust ANSOLYSEN dosage as necessary.[2,4] Home pressures should be taken with the patient in the standing position and at the time of maximum drug effect. For more complete information on this method, see package circular or other ANSOLYSEN literature.

Where taking of home blood pressures is not practical, control of dosage by symptoms[2] of hypotension is more useful than the taking of occasional blood pressures. If it is uncertain whether an effective dose is being maintained, it should be increased by 20 mg. increments cautiously until mild faintness occurs in the standing posture. Thus, control of dosage is in terms of hypotensive symptoms such as faintness or lightheadedness and not in terms of by-effects such as dry mouth or blurred vision.

Adjunctive Therapy: The concomitant use of reserpine with ANSOLYSEN produces smoother blood pressure response, decreases the dose of ANSOLYSEN required,[2] and minimizes by-effects from parasympathetic blockade.[5]

Precautions: ANSOLYSEN affects sympathetic and parasympathetic nerve transmission. Improper technique may result in marked postural hypotension, constipation, dryness of the mouth, blurred vision, urinary retention (especially in males with enlarged prostates), and, rarely, obstipation or paralytic ileus.

It is mandatory to maintain normal bowel function. Pilocarpine nitrate, 2.5 to 5 mg., taken with each dose of ANSOLYSEN, usually controls constipation, blurred vision, and dryness of mouth.[2] If pilocarpine fails to control constipation, 15 to 30 mg. of Prostigmin®[2] may be taken upon arising; if necessary, a laxative such as Petrogalar® with Phenolphthalein may be taken at bedtime. In the presence of constipation, the dose of ANSOLYSEN should be reduced until normal bowel function returns; then the dose should be gradually restored to the optimal level.

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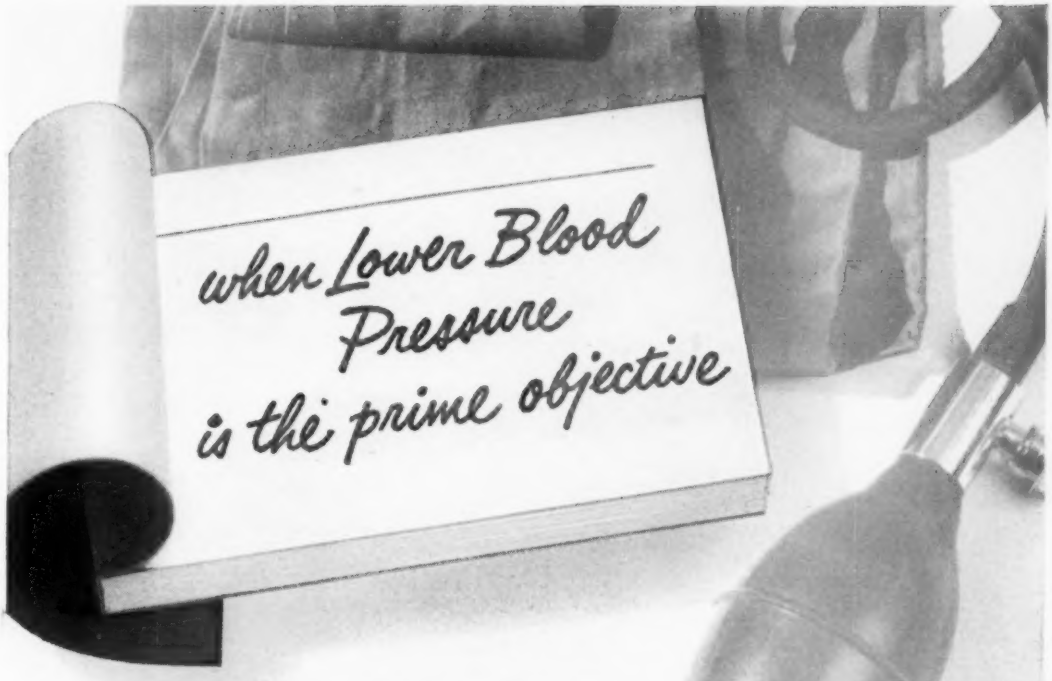

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1. Klohs, M. W.; Draper, M. D., and Keller, F.: J. Am. Chem. Soc. *76*:2843 (May 20) 1954.

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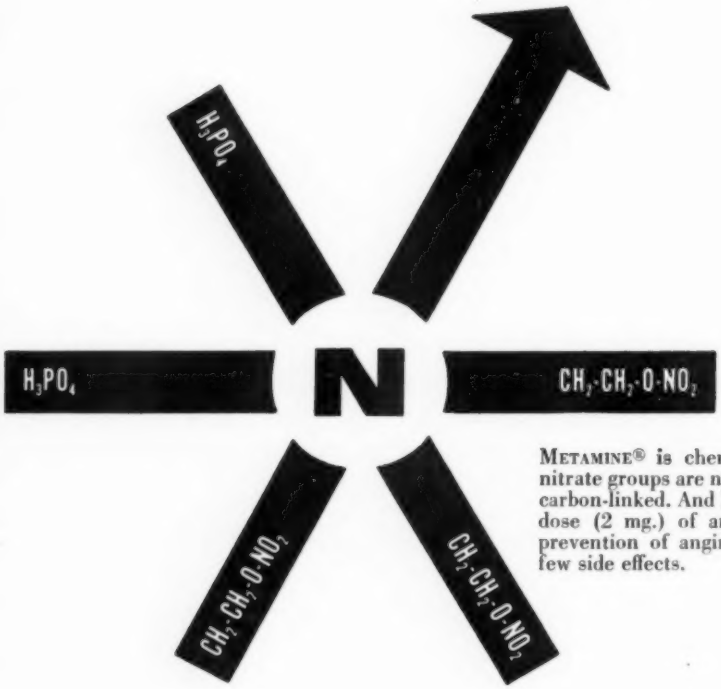

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1. *Palmer, J.J., and Ramsey, C.G.: Canadian M.A.J., 65:16, July, 1951; P. Dailheu-Geoffroy: La Clinique, 46:27, May 1951.*
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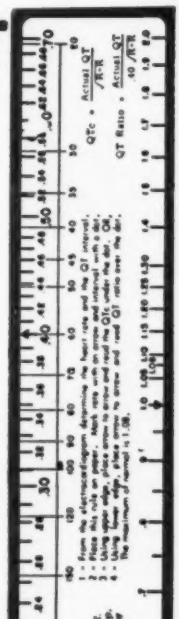

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American Heart Journal

For the Study of the Circulation

JONATHAN C. MEAKINS, M.D., Editor

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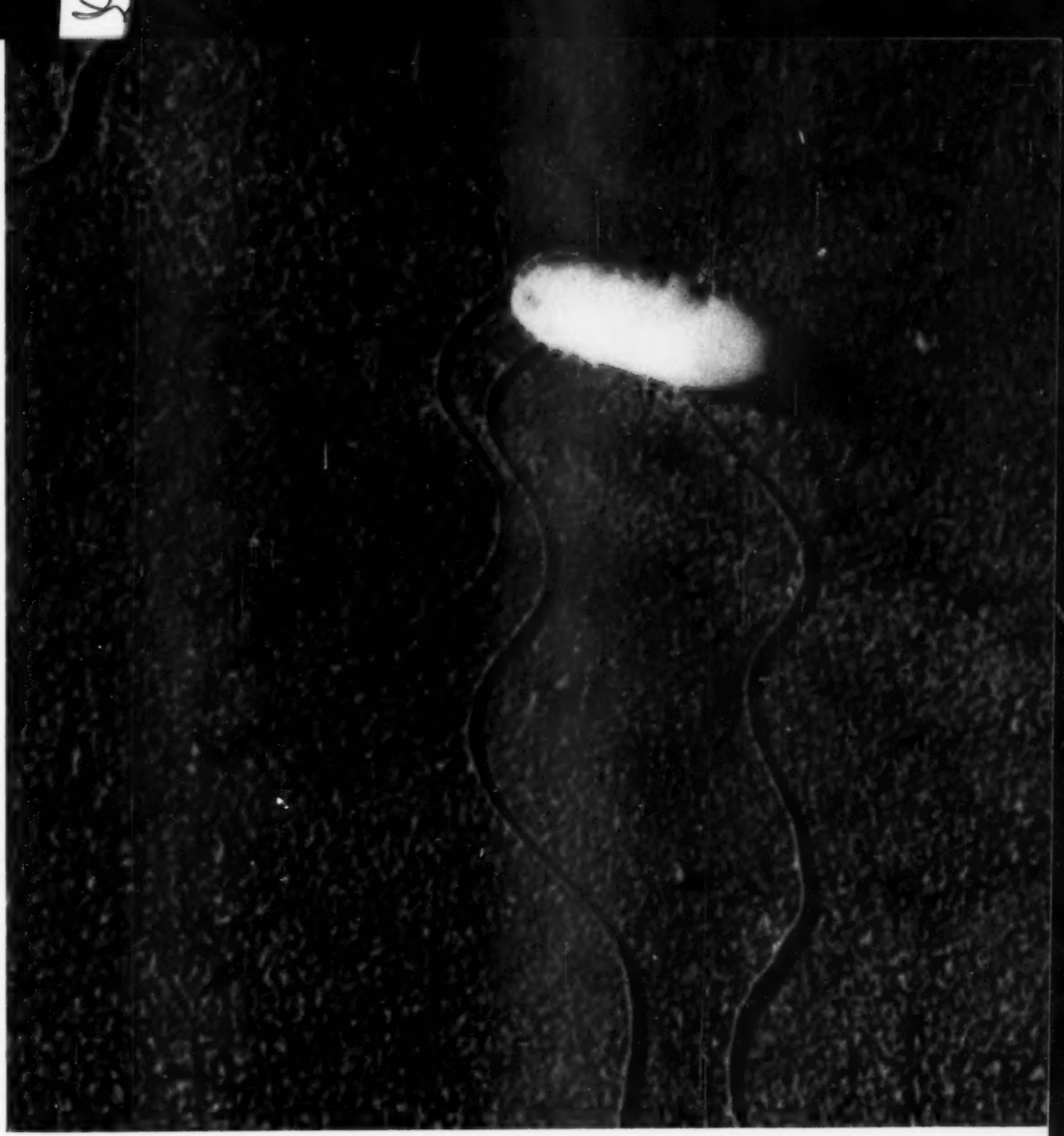

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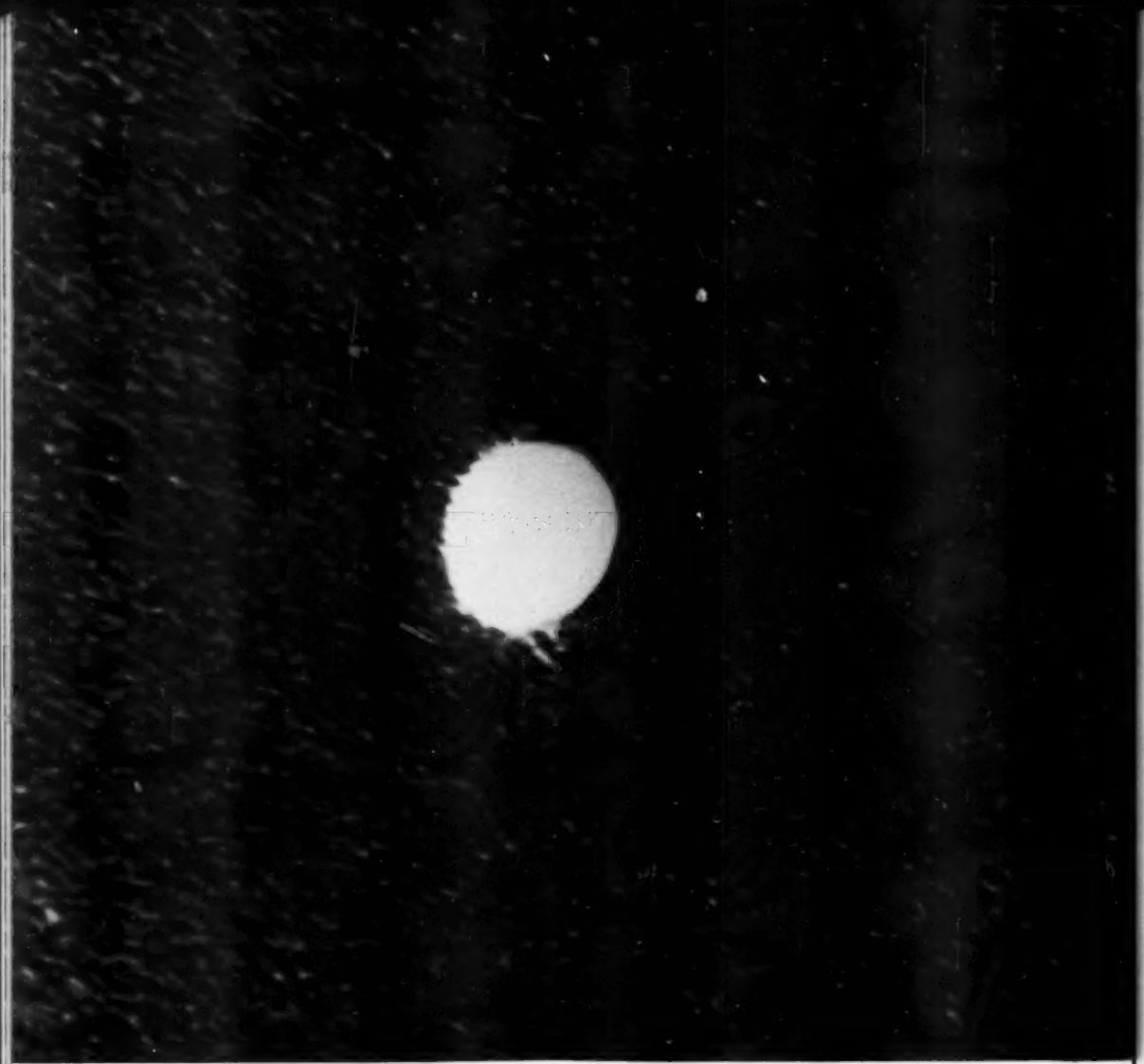

ELECTRON PHOTOMICROGRAPH

Staphylococcus aureus 35,000 X

Staphylococcus aureus (Micrococcus pyogenes var. aureus) is a Gram-positive organism commonly involved in a great variety of pathologic conditions, including

pyoderma • abscesses • empyema • otitis • sinusitis • septicemia bronchopneumonia • bronchiectasis • tracheobronchitis • and food poisoning.

It is another of the more than 30 organisms susceptible to

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BALLISTOCARDIOGRAPH

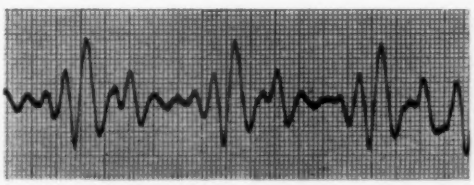
Instruments for both STANDARD and LATERAL Records—Dock[1-2]

The necessity of having lateral BCG's as well as the standard head-foot record in certain clinical situations is becoming apparent. Single plane ballistocardiography has been compared to single lead electrocardiography. A compact, two-inch high platform, to be placed under the thorax of the subject for lateral records has recently been described by Dock.[2] Full information on this instrument will be sent on request.

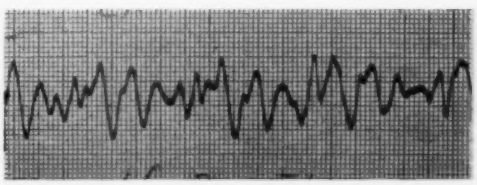
The search for the perfect ballistocardiograph continues. Practitioners have been offered a bewildering array of instruments. Direct body ballistocardiography is under fire, since not all oscillations are the result of cardiovascular activity. But no satisfactory aperiodic instrument seems a practical clinical tool as yet.

Attention has been focused on the deterioration of the BCG following smoking. My medical advisers emphasize that at the present time this can only be considered suggestive of occult coronary artery disease. The standard Dock instrument is admirably suited for the "cigarette test" as indicated below.

Resting BCG



Resting BCG following cigarette



G.S. A 29-year-old white male sustained 9 months previously an acute postero-lateral myocardial infarction. This was proven by serial ECG's. Serum cholesteral 410 mg. %. Recovery was uneventful, and there was no residual ECG or other evidence of coronary artery disease.

The resting BCG is normal. The deterioration of the tracing following a single cigarette is striking.

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MOBILE Table for BCG work	$195.00
Table alone	$145.00

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[1]Dock, W., et al., J.A.M.A. 146; 1248: Aug. 4, 1951
[2]Dock, W., Am. J. Med. Sci., 228:125: 1954
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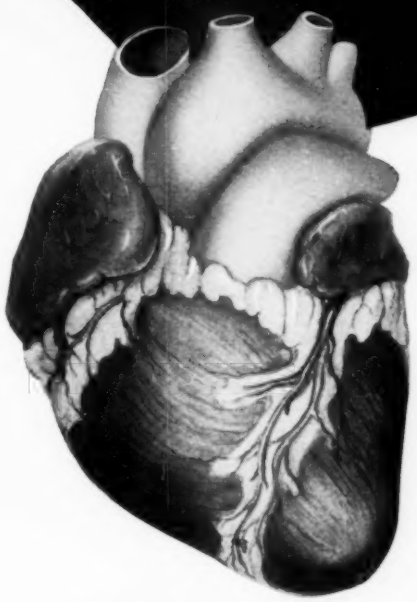

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Supplied:

Methium 125 with Reserpine—scored tablets containing 125 mg. of Methium and 0.125 mg. of reserpine.

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1. Ford, R. V., and Moyer, J. H.: Am. Heart J. *46*:754 (Nov.) 1953.
2. Crawley, C. J., *et al.*: New York State J. Med. *54*:2205 (Aug. 1) 1954.

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